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Contents of Volume XXVI.

Poul Flemming Møller. 1885—January 22nd—1945	*Carl Krebs*	7
The Malignancy of Giant Cell Tumors	*Sigurd Ry Andersen*	11
Vaso-seminal Vesiculography and its Clinical Application	*Arne Bertelsen* and *H. H. Wandall*	36
Some Practical Hints on the Performance of Urography on Infants	*Harald Christiansen*	46
On the Incidence of Osteochondrosis	*Sv. A. Chrom*	49
Invagination of the Stomach	*Kai Dohn* and *Børge Faber*	56
Case of Cleidocranial Dysostosis	*Helge Eltorm*	69
Le Forage de l'Épiphyse fémorale de Duvernay. Un examen complémentaire de 41 cas	*Jørgen Ernst*	76
The Value of Kymography for the Differential Diagnosis between Aneurysm of the Aorta and Mediastinal Tumor	*Bryan Fabricius*	89
Dosis Measurements in Roentgen Irradiation of the Female Pelvis	*Anton Jensen*	99
Some Cases of Intestinal Tuberculosis in Phthisics, with Reference Especially to the Prognosis	*Sv. Børre Larsen*	117
Roentgen Treatment of Malignant Tumors of the Nasopharynx	*Jens Nielsen*	133
Naevoépithélioma non pigmenté à l'évolution lente présentant une image histologique peu caractéristique	*Jens Munck Nordentoft*	155
Periodic, Spontaneously Remittent Volvulus and the Symptoms in Cases of Colon Elongatum	*Flemming Nørgaard*	163
On Bechterew's Disease from the Roentgenologic Point of View	*Kristian Overgaard*	185
On Reticulum Cell Saroma in the Bones	*Thomas Rosendal*	210
The Passage of Contrast Substances through the Hypopharynx	*Karl Søndergaard*	222
Physiologische Passagenverzögerung an der Cardia	*Franz Sørensen*	225
A Case of Primary Lung Cancer Presumably Arisen from an old Tuberculous Cavern	*Gregers Thomsen* and *Sv. A. Chrom*	230
Four Cases of Diaphragmatic Intumescence	*Aage Wagner*	239
Electroendothermy as an Adjuvant to Radiotherapy in Uterine Cancer	*S. Thorén*	249
Über das Röntgenbild bei tuberkulöser Salpingitis	*Wolfgang Magnusson*	265
The Diagnostic Use of Radioactive Common Salt	*Gunnar Sohrne*	279
Roentgen Cinematography as a Routine Method	*Bengt Holmgren*	286
On the Reduction of Ileal-Ileocolic Intussusception by Means of Contrast Enema	*E. Dahl-Iversen* and *Børge Fogh*	293
Röntgenologisch untersuchter Fall von Cancer Thymi	*Axel Renander*	297
A Method for Determining the Blood Pressure in the Pulmonary Artery	*Nils Westermark*	302
Roentgenographical Pulmonary Changes in Periarteritis Nodosa	*Tore Svanberg*	307

Plastic Induration of the Penis	*Kay Schourup*	313
Peripheres Aneurysma in der Art. pulmonalis	*Arne Clausen*	324
The Roentgenologic Differentiation between Hypertrophy of the Prostate and Vesical Uroliths	*Axel Renander*	329
A Case of Roentgenologically Observed Perirenal Oedema after Therapy with Sulphanilamide Preparations	*Olallo Morales*	334
Über die nomographische Berechnung von Röntgenlokalisationswerten	*Sölve Stenström*	339
On the Treatment of Malignant Tumours of the Testis	*Haakon Ödegaard*	345
Intensity Variations in the Field of Irradiation	*Viggo E. Thayssen*	353
Clinical Results with Rotation Therapy in Cancer of the Esophagus	*Jens Nielsen*	361
A Roentgen Cinematographic Study of the Movements of the Mitral Ring during Heart Action	*Henning Odqvist*	392
On Keloids and their Treatment	*Sverre Strand*	397
A Case of Ileocolic Intussusception Reduced without Operation	*Børge Faber*	409
Cancer Coli Multiplex	*Olle Olsson*	415
Tumoursimulating Intrathoracic Heterotopia of Bone Marrow	*Erik Ask-Upmark*	425
Adamantinomas of the Jaw, with Reference especially to their Treatment	*Karen Lübschitz*	441
Ein Fall von Thoraxdeformität, der als Folge angeborener Missbildung der Brustwirbelsäule aufgefasst wird	*Risto Elo*	456
Investigation into the Time Factor in the Roentgen Irradiation of Cancer Cells	*B. Refslund Poulsen*	463
On Osteoarthrosis Alkaptonurica (Ochronotica) with Description of one Case	*Johan Hertzberg*	484
A Rare Anomaly in the Elbow — Patella Cubiti	*P. M Kjelland*	491
An Attempt at the Roentgenologic Visualization of Coronary Blood Vessels in Man	*Stig Radner*	497
Über die Möglichkeiten der Röntgentherapie bei der Behandlung des Brustkrebses	*S. Mustakallio*	503
Studies on the Brown-Pearce Rabbit-Carcinoma with the Aid of Radioactive Isotopes	*A. Forssberg* and *F. Jacobsson*	523
The Roentgen Picture of the Tabetic Arthropathies and Affections of Bones	*P. Flemming Møller*	535
Necrosis of the Renal Papillae Following Retrograde Pyelography	*V. Eskelund*	548
On Radio-Surgery of Tumor Metastases in the Lymph Glands of the Neck	*Rolf Bull Engelstad*	555
Observations on the Technique of Phlebography	*Gunnar Bauer*	577
The Treatment of Tumors of the Urinary Bladder	*Rolf Weyde*	589

Index to Volume XXVI.

Roentgen Diagnostics.

Digestive Tract

	Pag.
Invagination of the Stomach	56
Intestinal Tuberculosis	117
Periodic Volvulus of Colon Elongatum	163
Hypopharynx	222
Cardia	225
Diaphragmatic Intumescence	239
Ileocolic Intussusception	293, 409
Cancer Coli Multiplex	415

Lungs, Pleura and Mediastinum.

Mediastinal Tumor and Aortic Aneurysm	89
Cancer from old Tuberculous Cavern	230
Cancer thymi	297
Pulmonary Changes in Periarteritis nodosa	307
Tumoursimulating Heterotopia of Bone Marrow	425

Heart and Vessels.

Aortic Aneurysm and Mediastinal Tumor	89
Measurement of the Blood Flow	279
Blood Pressure in the Pulmonary Artery	302
Periarteritis nodosa	307
Aneurysma der Art. pulmonalis	324
Coronary Blood Vessels	497

Diseases and Fractures of Bones and Joints.

Osteochondrosis	49
Cleidocranial Dysostosis	69
Le Forage de l'Épiphyse fémorale de Duvernay	76
Bechterew's Disease	185
Reticulum Cell Sarcoma	210
Tumoursimulating Intrathoracic Heterotopia of Bone Marrow	425
Adamantinomas of the Jaw	441
Thoraxdeformität und Missbildung der Brustwirbelsäule	456
Osteoarthrosis Alkaptonurica (Ochronotica)	484
Patella Cubiti	491
Tabetic Artbropathies	535

Uro-Genital System.

Vaso-seminal Vesiculography	36
Urography in Infants	46
	Pag.
Tuberkulöse Salpingitis	265
Hypertrophy of Prostate and Vesical Uroliths	329
Perirenal Oedema	334
Necrosis of the Renal Papillae	548

Radiotherapy.

Giant Cell Tumors	11
Malignant Tumors of the Nasopharynx	133
Naevoépithélioma non pigmenté	155
Uterine Cancer	249
Plastic Induration of the Penis	313
Malignant Tumours of the Testis	345
Rotation Therapy in Cancer of the Esophagus	361
Keloids	397
Adamantinomas of the Jaw	441
Brustkrebs	503
Radio-Surgery of Metastases in Lymph Glands	555
Tumors of the Urinary Bladder	589

Radiobiology.

Time Factor in Irradiation of Cancer Cells	463
Rabbit Carcinoma and Radioactive Isotopes	523

Technique.

Roentgen Examination.

Diagnostic Use of Radioactive Common Salt	279
Roentgen Cinematography	286
Blood Pressure in the Pulmonary Artery	302
Röntgenlokalisation	339
Cinematographic Study of the Mitral Ring	392
Phlebography	577

Radiotherapy.

Dosis Measurement in Irradiations of the Pelvis	99
Intensity Variations in the Field of Irradiation	353

Personalities.

Poul Flemming Møller	7

List of Authors.

Cited in Volume XXVI.*

Aaron 237
Abel 421
Abels 531
Adams 60
Adati 463, 480
Agati 59
Ahlbom 504
Ahlfeld **457**
Ahlström 210, 216, 235
Aimes 76
Åkerlund 242, 278
Albrecht 484
Alexander 457
Alibert 397
Alpers 441
Altschul 203
Andersen **11**
Arneson 114
Ascher 74
Aschoff 437
Ask-Upmark **425**
Assman 324
Atterling 282

Bachmeister 123
Baclesse 103
Baensch 225, 398
Balfour 60
Bang 139, 345
Bargen 417, 421
Bauer 74, 464, 484, **577**
Bayle 237
Beato 100
Bechterew 185
Behan 505
Behrendt 236
Belfield 36, 43
Bellot 400
Bender 105
Bergendahl 558
Bergstrand 337, 553
Berkson 347
Bernard 560, 565
Bernasconi 317
Bernays 444
Berntsen 77, 80
Bertelsen **36**, 38
Berven 99, 151, 249, 503, 514, 558, 562
Beykirch 493, 494
Bignami 60
Billmann 237
Billroth 415
Björkman 309
Blaisdell 427
Blanchard 536, 544
Blothner 517
Blumgardt 279
Boas 59
Boehm 203, 456, 457
Boels 122
Bonchet 249
Bonomini 60
Bordier 249
Borrman 415
Borst 415, 441
Bosselman 427
Böttner 457
Bowen 371
Brannan 426, 434, 437
Brites 437
Broders 505
Bronchhorst 119
Brown 118, 524
Browder 219
Brunner 117
Buchert 345
Buckley 191
Buntiug 478
Buschke 21

Cabot 347
Caldas 497
Cameron 60
de Carvalho 497
Casey 524
Caspersson 524
Cassidy 225
Castellanos 497
Chaikoff 529
Chaoul 104, 106, 402
Chaperon 90
Charcot 535
Charry 77
Chenal 492
Chibret 444
Chievitz 28, 100
Christensen 409
Christiansen **46**, 119, 141
Christie 298
Chrom **49**, **230**
Chydenius 100
Clausen **324**
Cokkinis 416
Coley 13
Collin 16
Collins 427
Colston 317
Cone 437
v. Conta 308, 311
Cooper 236
Cooperman 434
Copeland 11, 29, 194, 216
Coquelet 565
Coutard 143, 150, 376, 557
Crafoord 423
Craver 216, 218
Crile 563
Critchley 441
Cunha 437
Curtis 445
Cutler 21, 99, 152

Dahl 559, 562, 566
Dahl-Iversen 293, 294
Dawid 120
Davidson 219
Dawson 427, 434, 437
Day 211
Degrait 400
Dehn 120
Dekker 203
Delherm 90
Desenfants 494
Desjardins 345, 348
Dessauer 101, 105
Dietrich 426
Dobson 346

* *The full-faced figures refer to original articles.*

Dohn **56**
Döring 216
Dorneich 354
Drexler 100
Drybrough 249
Duvernay 76
Dwyer 298

Ebbenhorst 191, 203
Edberg 409
Ederlen 59
Edling 211, 216
Edwards 216, 244
Elo **456**
Eltorm **69**
Engel 60
Engelbreth-Holm 16, 33, 211
Engelmann 74, 118
Engelstad 349, **555**, 558, 562, 593
Erf 531
Ernst **76**
Eskelund **548**
Eusterman 60
Ewald 493, 494
Eve 443
Ewing 13, 100, 216, 237, 238,

Faber **56**, 409
Fabricius **89**
Fabricius-Möller 56
Falkenfleth 237
Falkson 441, 443
Faulhaber 119
Feinbrunn 445
Feleky 317
Fetzer 90
Fillenz 329
Fischer 441
Fiske 91
Flax 105, 106
Fleischer-Hansen 16
Fleischner 119
Foged 73
Fogh **293**
Fog-Möller 61
Foot 221
Forssberg 464, 470, **523**
Forrestier 86, 186
Forssell 120, 503, 514
Fraenkel 185, 193
Fratin 426
Frazier 441
Fredholm 281
Fredzell 281
Freund 399
Fried 235
Friedl 225
Friedrich 100, 302
Fuss 400

Gabriel 421
de Gaetani 517
Gage 457
Gale 244
Galewski 317
Garcia 497
Gard 324
Garrod 211
Gellerstedt 485
Genner 313
Gerlach 265
Geschickter 11, 29, 61, 194, 217
Gershon-Cohen 119, 122
v. Gierke 427
Girard 77, 81
Godtfredsen 135
Goetze 415
Goforth 14
Goldzieher 211
Gonnermann 845
Goormaghtigh 210
Graber-Duvernay 76
Grabowski 203
Graham 237
Gram 119
Grauer 492
Grevillius 346
Grimmet 463, 480
Groedel 90
Groover 298
Groth 164
Gubner 92
Guensel 105
Guentz 188, 195
Guérin 427
Gunn 494
Gutman 207
Gylstorff-Petersen 519

Haas 329
Hackenbroch 77
Hadfield 211
Haenisch 203
Hagner 43
Halsted 503
Hamann 313, 314
Hamant 77, 81
Hamburger 345
Hamilton 237, 523
Hampel 308
Hansson 504
Harpoth 457
Harrington 504, 520
Hartfall 427, 434
Hasché 354
Hawley 105
Hebbel 441
Hellmer 294, 410, 414, 422
Hellner 11, 15
Hellsten 578, 587
Henriques 107
Henschen 59, 324
Henschke 105
Herendeen 15
Herrman 308, 311
Hertzberg 122, **484**
Hesse 443
Heuser 36
Hevesy 280, 523
Heyman 99, **249**, **253**, 256
Higgins 345
Hinman 346
Hintze 397
Hirsch 299
Hodgkin 211
den Hoed 354
Hoeffer Jensen 105
Hofstätter 427, 437
Holfelder 370
Holm 286, 287
Holmgren **286**
Holst 324
Holthusen 354
Holzkneckt 358
Honeybourne 100
Howes 100
Huber 266
Huitfeldt 313
Hultén 485
Hultkranz 73
Hunter 427, 434
Hurdon 100
Husfeldt 230, 234
Husted 237
Hybbinette 76, 80, 83, 86.

Ironside 441
Isager 237
Ivy 445

Jacchia 324
Jaches 457
Jachmann 316
Jackson 216
Jacobs 444
Jacoby 409
Jacobsson **523**
Jaffe 31, 237
Jalet 324
Jamieson 345
Jansen 73
Japiot 494
Jensen, A. 59, **90**, 368
Johnsson 423
Jones 457, 529
Junghans 49
Juul 102, 463

Kahlmeter 203
Kalima 505
Kallós 524
Kaplan 558
Katz 493
Kaufmann 117
Kegerreis 339
Kehmen 203

Keibel 457
Kemp 59, 463
Kennedy 558
Kenney 531
Kermauner 100
Kersley 203
Keysser 249
Kienböck 89, 456, 484, 491, 494
Kimmerle 89
Kirchhoff 100
Kjelland **491**
Kjellberg 16, 265, 589, 583, 585
Kleinschmidt 485
Kline 122
Klinge 188
Knehn 191
Kneise 329
Knutsson 49
Kock 409
Köhler 494, 503
Köhlmeier 216
Krabbe 73
Krebs 189, 191, 203
Kredel 537
Kremser 494
Krompecher 442
Kronfeld 442, 444
Kudlich 427
Kuehlman 203
Kuestner 356
Kundrat 100
Küttner 556

Lacassagne 100, 557
Lacharité 15, 31
Lamaris 100
Lamas 497
Lannec 237
Laqueur 89
Larsen **117**, 313
Lassen 191
Laurell 167, 392, 409
Lawrason 118
Lawrence 280, 529, 531
Lecaplain 457
Leddy 345, 348
Lehmann 77, 80
Leishman 307
Lenk 90, 297, 497
Leriche 76, 426
Levene 497
Lidström 77
Lieberknecht 457
Lima 497
Lindblom 578, 583, 585
Livingston 503
Loepp 218
Lönnerblad 59, 62
Lotsch 59
Lucinesco 426
Lund 314
Lundquist 277
Lundsgaard 226
Lyall 427
Lübschitz **441**
Lysholm 287

Macfarlane 60
Madsen 101, 266
Magitot 443
Magnusson **265**
Maingot 417, 421
Malassez 443
Mall 457
Mallet 105
Martin 73
Maseritz 217
Mathey-Cornat 100
Matz 237
Maximow 426, 437
Mayer 105
Maylcord 100
Mc Gregor 443
Meissner 60, 65
Melnikowa 494
Meltzer 223
Merricks 43, 38
Merrit 298
du Mesnil de Rochemont 105
Meyer 91, 92, 105, 503
Miyakawa 105, 361, 364
Michaels 219
v. Miculicz-Radecki 249
Minder 101
Minnes 61
Mittchell 535
Møller 16, 119, 172, **535**
Moniz 497
Monod 557
Morales **334**
Morestin 563
Motida 463, 480
Mudd 104
Muscer 318
Mustakallio **503**
Myhre 60
Müller 423

Nakaidzumi 105, 361, 364
Nauck 495
New 444
Nielsen, J. 102, 105, **133**, 219, 345, 348, **361**
Noechel 120
Nohrman 519
Norbury 421
Nordentoft **155**, 293, 410, 413
Nørgaard **163**, 171
Norman 65
Nuvoli 498
Nyborg 293
Nylander 244
Nylin 280

Oberling 210, 217, 427
Ödegaard **345**
Odessky 494
Odqvist **392**
Oliver 441
Olsen 28
Olsson **415**
Onanoff 441
Ørum 409
Overgaard 49, **185**

Pack 503
Padovani 77
Paltauf 73
Palugyay 329, 331
Pancoast 298
Pannenitz 203
Pansdorf 120
Papadamitriou 442
Parker 216
Pauly 493
Paus 416
Payer 118
Payne 347
Pearce 524
Pearl 237
Pereiras 497
Petrén 423
Petri 427, 436
Pfahler 504
Pfitzner 491
Philipp 266
Picena 211
Pierquin 557
Pierre Marie 73, 185
Pikkarainen 505
Plonskier 427, 434, 437
Pohl 105
Pohle 478
Policard 76
Pouliquen 409
Prout 105
Putti 457

Quimby 114

Rabin 457
Rabinowitsch 299
Radner **497**
Rahm 105
Rankin 417, 421
Raubitscheks 74
Refslund Poulsen **463**
Del Regato 152
Regaud 100, 101, 557, 558, 562
Regnard 536, 544
Reichenmiller 100
Reid 497
Renander **297**, **329**
Retz 397
Reynes 76

Rezsö 317
Rich 427, 434
Richard 557
Richardson 427
Rieder 225
Robb 497
Robertson 478
Robinson 441, 443, 444
Rokitansky 237
Rolnick 36, 43
Rosendal **210**
Rostock 494
Roulet 210
Rousthöi 498
Rouvière 556
Roux-Berger 557, 560, 562, 564, 567
Runström 274
Rusby 89

Sacerdotti 426
Sainton 73
Saleeby 427, 433
Sampson 118
Sandberg 567
Santesson 524
dos Santos 497
Sargent 37, 41, 43
Sauerbruch 243
Schanta 100
Schatzki 89
Schedtler 457
Scheel 567
Schenthauer 73
Schinz 15, 152, 225, 463
Schlange 457
Schmidt 92, 444
Schmieden 416
Schmorl 49, 456, 457, 461
Schmitzler 427, 437
Schober 329
Schoenberg 91
Schourup **313**
Schultze 265
Schwalbe 236
Scott 92, 191, 193, 203, 441
Senty 60
Shay 119
Sherman 400
Siccard 36
Sievert 100, 354, 464, 470
Simon 457
Simons 398
Sivon 188
Sjöström 409
Slotpolski 463
Smereker 100
Snyder 203
Söderlund 244, 423
Sohrne **279**
Søndergaard **222**
Soper 225
von Soos 427, 436
Sørensen **225**
Spear 463, 480
Stang 558
Stein 235
Steinberg 497
Steinthal 505
Stenström **339**
Stewart 13, 427, 434
Stierlin 119, 122
Stoeckel 249
Stone 15
Strand **397**
Struempel 185
Strunge 478
Stumpf 90
Swaim 191
Svanberg **305**

Tailhefer 562, 564, 567
Tammia 51
Tengbergen 191, 203
Thayssen **353**
Thomsen 59, **230**
Thorén **249**
Tigerstedt 302
Tillesen 492
Tisell 120, 311
Todd 104
Touw 203
Truelsen 100
Tuttle 531

Uebermuth 484
Ungerleider 92

Wachsmann 104
Wade 426, 437
Wagner 237, **239**
Wahl 324
Wahlgren 277
Waldenström 289
Valentin 73
Walldén 48
Walther 457
Walton 61
Wandall **36**
Varnek 38
Warnekros 101
Warren 211, 427
Wasserburger 100
Waters 317
Waxelbaum 553
de Veer 219
Weiser 317
Weiss 279
Weiszaecker 544
Weltz 90
Ventz 203
Wessler 457
Westermark 230, **302**
Wexler 237
Weyde **589**
Wichmann 409
Videbæk 372
Widman 558
Wilhelm 37, 43
Wilkens 324
Williams 399
Wilms 544
Wilson 237
Winckler 492
Wintz 100
Virchow 484, 492
Wissenberg 105, **357**, 368
Wissing 49
Vogt 49
Wolf 237
Voltz 100
Worning 235
Wrete 436
Vrolik 457
Wurm 189, 207

Young 434
Ylppö 461

Zdansky 59, 62
Zdarek 484
Zimmer 101
Zintheo 354
Zislin 313
Zuppinger 15, 140, 152, 354

Å, Ä, see A

Ö, see O

THE

FLEMMING MØLLER

BIRTHDAY BOOK

STOCKHOLM 1945

THIS VOLUME IS DEDICATED TO

POUL FLEMMING MØLLER, M. D.

PROFESSOR OF RADIOLOGY AT THE UNIVERSITY OF
COPENHAGEN ON THE OCCASION OF HIS SIXTIETH
BIRTHDAY JANUARY TWENTY-SECOND, 1945, BY
HIS FORMER AND PRESENT PUPILS AND
COLLABORATORS AS EXPRESSION
OF THEIR FRIENDSHIP AND
IN ACKNOWLEDGMENT
OF HIS VALUABLE
TEACHING

Hermann Bahr

THE FOLLOWING HAVE CONTRIBUTED TO THE EXPENSES FOR PUBLICATION OF THIS BOOK

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INDEX.

Poul Flemming Møller. 1885 — January 22nd — 1945 by Carl Krebs 7
The Malignancy of Giant Cell Tumors by Sigurd Ry Andersen 11
Vaso-seminal Vesiculography and its Clinical Application by Arne Bertelsen and H. H. Wandall 36
Some Practical Hints on the Performance of Urography on Infants by Harald Christiansen 46
On the Incidence of Osteochondrosis by Sv. A. Chrom 49
Invagination of the Stomach by Kai Dohn and Børge Faber 56
Case of Cleidocranial Dysostosis by Helge Eltorm 69
Le Forage de l'Épiphyse fémorale de Duvernay. Un examen complémentaire de 41 cas par Jørgen Ernst 76
The Value of Kymography for the Differential Diagnosis between Aneurysm of the Aorta and Mediastinal Tumor by Bryan Fabricius 89
Dosis Measurements in Roentgen Irradiation of the Female Pelvis by Anton Jensen 99
Some Cases of Intestinal Tuberculosis in Phthisics, with Reference Especially to the Prognosis by Sv. Børre Larsen 117
Roentgen Treatment of Malignant Tumors of the Nasopharynx by Jens Nielsen .. 133
Naevoépithélioma non pigmenté à l'évolution lente presentant une image histologique peu caractéristique par Jens Munck Nordentoft 155
Periodic, Spontaneously Remittent Volvulus and the Symptoms in Cases of Colon Elongatum by Flemming Nørgaard 163
On Bechterew's Disease from the Roentgenologic Point of View by Kristian Overgaard 185
On Reticulum Cell Sarcoma in the Bones by Thomas Rosendal 210
The Passage of Contrast Substances through the Hypopharynx by Karl Søndergaard 222
Physiologische Passagenverzögerung an der Cardia von Franz Sørensen 225
A Case of Primary Lung Cancer Presumably Arisen from an old Tuberculous Cavern by Gregers Thomsen and Sv. A. Chrom 230
Four Cases of Diaphragmatic Intumescence by Aage Wagner 239

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POUL FLEMMING MØLLER

1885 — January 22nd — 1945

The first chair of medical radiology at the University of Copenhagen was established in 1930. Also before that time some instruction in the new science had been given, but it had been incidental and spread. JOHAN FR. FISCHER had for many years been an excellent director of the roentgen services of the municipal hospitals of Copenhagen, and a watchful, intelligent pioneer,[1] especially in roentgen therapy. At the Finsen Institute, AXEL REYN had carried the light therapy forward in a worthy manner, and at the State Hospital H. J. PANNER had striven steadfastly for improvement of roentgen diagnosis in those first, difficult years.

Chairs of radiology were being established at the universities in the different countries; Sweden had had one already for several years. In Denmark, the possibility of a similar establishment had long been discussed. PANNER hesitated from accepting the charge; he had for several years held brief series of lectures, but did not feel his health strong enough for the greater responsibility.

FLEMMING MØLLER became the first appointed lecturer in medical radiology at the University of Copenhagen, and at the same time head of the roentgen clinic at the State Hospital. To the last-named post he brought the results of a thorough and clinically all-round training. In 1916, five years after he had graduated in medicine, he had become

assistant, first to FISCHER, afterwards to PANNER; from 1920 to 1930 he had been head of the roentgen clinic of the Frederiksberg Hospital, in which position he won general recognition as an excellent diagnostician and by his exceptional technical abilities. During those years he wrote, as thesis for the degree of M. D., what is until now his most outstanding contribution to medical radiologic literature, a study on CALVÉ-PERTHES' disease (malum deformans coxae infantile), in which he definitely established the clinical and roentgenologic picture of that affection. He has since during many years closely followed the cases mentioned there, and has shown that the prognosis of the disease was not as good as it had been thought, as many of these cases were followed by even considerably deforming arthritis, which made the patients more or less invalids.

FLEMMING MØLLER has been a very diligent writer. Besides the work just named, his literary output until now consists of twenty-two larger and smaller papers, most of them dealing with questions of roentgen diagnosis. In the last years, three subjects, particularly, have engaged his attention: fluorine poisoning, silicosis and the roentgen picture of the tuberculous intestine, as contrasted with that of simple colitis and cancer. To the roentgen picture of fluorine poisoning in cryolite workers, his name will always remain attached as the first who established that picture and the etiology of the disease. At the same time, he described (together with SKULE GUDJONSSEN) the other aspects of its pathologic picture: the stomach affection and the pulmonary changes. With silicosis, he has dealt in three papers (1927, 1934 and 1940), in which he describes in detail the roentgen picture of the disease and thoroughly discusses its diagnosis from tuberculosis and other affections of the lung. In other papers on pulmonary affections he has dealt with such subjects as lung cysts and pleura thickenings, and he was one of the first to introduce bronchography. About roentgen therapy he wrote, in 1928, an orientating paper, in which he particularly emphasized the importance of rational measure-

ment and calculation of the depth dose; and in 1924 he described the roentgen picture of myelomatosis. Finally, he has published a number of studies based on special cases, for instance of non-acute perforations from the gastrointestinal tract, and has made numerous contributions to the discussions in the Danish Radiologic Society.

As said, it became the privilege of FLEMMING MØLLER to lay the foundations of the instruction in radiology in Denmark. In his lectures he deals especially with the diagnosis. His courses fall in the third semester after the students have passed their first examinations; that is at a time when their clinical and patho-anatomic knowledge is not very great; and without at least a certain familiarity with those subjects a part of the instruction in radiology must necessarily fall on stony ground. FLEMMING MØLLER has understood this, and has therefore introduced a repetition course during the last semester before the final examinations, which is of great value for the physicians-to-be.

One of FLEMMING MØLLER's best qualities, besides those displayed in his scientific writings, is his critical sense. As university teacher he has had occasion to review a great many scientific works. His opposition at the M. D. disputations has always borne the mark of careful preparation; one feels that he has really worked with the subject and has tried to see it in a new light; and he understands to shift wind and sun equally in a calm and objective manner.

The lines he has laid down for the instruction in roentgen diagnosis at the University of Copenhagen are being followed with good results at the much younger University in Aarhus. It might perhaps be wished that some more time could be given to the therapy.

As diagnostician, FLEMMING MØLLER is absolutely the leading in Denmark. One feels this nearly every time he takes part in a discussion, and most do his collaborators feel it in the daily work at the roentgen clinic. His care and his ability to interpret a radiogram are unique.

On FLEMMING MØLLER's sixtieth birthday anniversary, Danish Radiologists wish to thank him because he has always done his best to raise the standard of the medical profession and advance radiology, for his lucid teaching, his critical sense, and last, but not least, for his good fellowship.

Carl Krebs.

FROM THE RADIUM CENTER, COPENHAGEN (CHIEF: JENS NIELSEN, M. D.) AND THE SURGICAL SERVICE OF THE FINSEN INSTITUTE (CHIEF: PROF. O. CHIEVITZ)

THE MALIGNANCY OF GIANT CELL TUMORS[1]

A Study on Giant Cell Tumors and Allied Affections in Bone, with Reference Specially to their Malignancy

by

Sigurd Ry Andersen

The malignancy of giant cell tumors is a controversial subject; which is not surprising, since the nature of these affections and their delimitation from a number of other benign and malignant affections in bone are still uncertain. In the last twenty years a great deal has been written about them: for particulars, GESCHICKTER & COPELAND's excellent: »Tumors of Bone» (New York, 1936) and HELLNER's: »Die Knochengeschwülste» (Berlin, 1938) may be referred to. Here, I shall call attention only to a few points of particular importance in connection with the subject.

The best known theory respecting the *pathogenesis* is the one advanced by GESCHICKTER & COPELAND, according to which the giant cell tumors and osteitis fibrosa are not true neoplasms, *but an abnormally highly developed phase of the normally occurring absorption of calcified cartilaginous tissue* which takes place during the normal endochondral growth of the bones preformed in cartilage. This absorption takes place by means of giant cells —osteoclasts — whose proliferation should be abnormally great owing to traumatically determined nutritional disturbances in the bone.

In the epiphyses of the long tubular bones, in which the vascular supply is poorest, there should, as a result of this, develop the more progredient forms, called *giant cell tumors;* histologically characterized by numerous giant cells with centrally situated nuclei and abundant hemorrhage, but only slight fibril formation and little, or no formation of new bone. The meta- and diaphyses, whose nutrition is better, should offer better conditions for a restorative reaction, resulting in the devel-

[1] Read, in a somewhat modified form, at the meeting of the Danish Radiologic Society, Feb. 9th, 1944. Submitted for publication, Aug. 25, 1944.

opment of *local osteitis fibrosa*, mostly in the form of an isolated *bone cyst* histologically characterized by a stroma rich in fibrils and with new bone formation, but only few giant cells and little hemorrhage; besides, there may be formation of cysts, because the bone tissue after resorption of hemorrhage cannot collapse. This restorative reaction, which is termed *fibro-ostosis*, should be furthered by the thicker cortex of the diaphyses, which forms a barrier against the abnormally proliferating tissue containing the osteoclasts; and the same should apply, though in lesser degree, to giant cell tumors in the head, vertebrae, ribs and fingers; which should explain the intermediate histologic forms often seen in those sites. According to GESCHICKTER & COPELAND, giant cell tumor and osteitis fibrosa should thus be two phases of the same disease, and in accordance with this conception they also term them respectively *progressive and regressive osteoclasia*.

According to this theory, the formation of giant cell tumors is connected with the development of the bones preformed in cartilage; and, in fact, they are found exclusively — or, at any rate, almost exclusively — in these. An exception to this are, however, the giant cell tumors — *epulis gingivae* — formed along the alveolar borders (which are preformed in connective tissue). GESCHICKTER & COPELAND consider these as entirely homologous formations, only connected with the normal resorption of the deciduous teeth by odontoclasts; and in support of this they point to the fact that epulis hardly ever occurs back of the first molar. With regard to the giant cell tumors that not rarely occur in, or near tendon sheaths in the hand and foot, they believe that they arise from sesamoid bones.

Generalized osteitis fibrosa (*Recklinghausen's disease*) is now held to be caused by hyperparathyroidism, most often a parathyroid adenoma, with secondary changes in the calcium- and phosphorus levels of the blood, and in the bones, where not only extensive halisteresis and multiple diaphyseal cysts are seen, but sometimes also epiphyseal giant cell tumors of a histologic structure similar to that of the solitary. It is even stated that the disease may begin with a giant cell tumor or an epulis. As a rule, removal of the adenoma will cure the disease, whereupon the changes in the bones disappear.

GESCHICKTER & COPELAND have, on the basis of a very large material, *maintained that a giant cell tumor always is benign*, and that in cases where metastases appeared and death supervened the diagnosis must have been wrong, in the sense that an original osteogenic sarcoma had not been recognized, or that the death was due to some other cause. In recent years they seem, however, to have had some doubts; and in the last edition (1936) of their work they relate a case which seems clearly to show malignant transformation of an originally benign giant cell tu-

mor. The theory proposed by the two authors seems very plausible and no doubt contains many correct observations; besides, it is the only one, so far, by which it has been possible to give a picture embracing both giant cell tumor and osteitis fibrosa. It has, therefore, also many adherents, though up to the present it cannot be said to have been proved.

While it is commonly agreed that osteitis fibrosa is not a genuine neoplasm, but always a benign affection (albeit from time to time cases of osteogenic sarcoma are reported, which have resembled benign bone cysts and have been treated as such), it is *maintained by many that giant cell tumors are true tumors, mostly benign, but in some cases malignant* (W. B. COLEY, J. EWING, F. W. STEWART). Others (H. L. JAFFE and co-workers) would among the epiphyseal giant cell tumors in long tubular bones recognize *a separate group, which they conceive as genuine neoplasms of varying malignancy.* They have even subclassified these tumors into three grades, according to the degree of their malignancy; rather on the line of BRODERS' system for grading of cancer. The weight is laid chiefly on the degree of differentiation of the stroma; the giant cells being considered as a more secondary phenomenon. Only typical giant cell tumors are recognized, while the numerous "variants" of such are left out. Their classification is as follows:

Grade I. Typical giant cell tumors of absolutely benign appearance, with numerous multinuclear giant cells with centrally situated nuclei and a »not compacted» stroma of chiefly round or oval cells with slight fibril formation; slight cellular atypism, no, or at most a few, normal mitoses. Furthermore, abundant hemorrhage and deposit of blood pigment, but only very slight new bone formation.

Grade II. Tumors with compacted stroma and marked atypism with rather frequent abnormal mitotic figures, perhaps also the giant cells somewhat atypical.

Grade III. Tumors with sarcomatous stroma with highly atypical cells and small giant cells.

Grade I corresponds to typical giant cells and are stated mostly to remain benign, but often to recur, and then to exhibit characteristics which put them in the next grade. The tumors of grade II correspond in appearance most nearly to the »malignant giant cell tumors», and are stated to have considerable tendency to recur, and in some cases to become malignant. The tumors of grade III are stated to be malignant, and to metastasise sooner or later.

The classification seems to me to be rather artificial, particularly as regards grade III, which in my opinion is only an expression for an osteogenic sarcoma with giant cells; a by no means uncommon finding. — The authors point out that the roentgenologic picture may be the same in all three grades, and stress the necessity of biopsy being performed in all cases.

As basis for their classification they have only a material of 14 sure cases of epiphyseal giant cell tumor, all in subjects above the age of 21 years. Of these, 3 are stated to have become malignant and ended in the patients' death. A closer scrutiny of the material shows, however that only with regard to the first of the cases is the documentation sufficient to make it acceptable as proof; and even so, the original microscopy classed it as grade II; that is as not indubitably benign.

Interesting, but somewhat lacking in clarity is a paper by F. W, STEWART & co-workers, relating some cases of so-called *»malignant giant cell tumor»*, which clinically and roentgenologically resembled benign giant cell tumors, but in which the first microscopy nevertheless showed very slight signs of malignancy, mostly in the form of single abnormal mitotic figures; the malignancy eventually being confirmed by the appearance of metastases and the death of the patients from malignant sarcomas containing giant cells. Unfortunately, no photographs of the preparations are given. The authors do not themselves draw any final conclusions from the material. It is possible that these somewhat dubious »malignant giant cell tumors» were merely osteogenic sarcomas, perhaps of a special type. On this point, there is need of further investigations; but the cases may serve as a reminder always to make thorough histologic examination, and in case of doubt to repeat the biopsy. EWING concludes (with GOFORTH) that »there are all degrees of malignancy; each must be evaluated according to its particular structure».

In the course of years a number of cases have been reported, about which it has been *maintained that malignant transformation of benign giant cell tumors into sarcoma has been proved*. In hardly any of them the proofs are satisfactory. It must be an absolute requirement that the original tumor is beyond all doubt benign, not only clinically and roentgenologically, but also histologically. Especially must it be pointed out that both chondrosarcomas and osteogenic sarcomas may give an exactly similar roentgenologic picture. Furthermore, it would be best to require that some years shall have elapsed before the malignant process manifests itself; since otherwise it is difficult to exclude the possibility that the growth is a primary osteogenic sarcoma. In the malignant stage there must often be required the occurrence of metastases of indubitable histologically malignant character; because a giant cell tumor often, if it has become infected or has been the object of several operations or irradiations, gets another, seemingly more malignant appearance. Nor yet can invasion of giant cell tumor tissue into the surrounding soft tissues be taken as proof of malignancy, since such invasion often occurs also in the case of otherwise benign giant cell tumors. In going through a number of cases from the literature I have found at any rate three that seem rather convincing. The first is GESCHICKTER & COPELAND's

case, already mentioned, of a giant cell tumor in the upper part of the tibia of a man, 45 years old, who three years after curettage and postoperative roentgen treatment had to undergo amputation for an osteogenic sarcoma. The other two — in which photomicrographs are lacking, though — are reported by W. B. COLEY (his cases no. 1 and 5). In the first, the growth was situated in the lower part of the femur of a man 39 years old, and had been treated by curettage and postoperative roentgen. In the other, it was situated in the upper part of the tibia of a man aged 19 years, and had been treated by curettage followed by radium (formerly published by STONE & EWING).

Besides, there are a number of cases in which the malignant transformation seems likely, but has not been proved. That such transformation may, in fact, occur, is also recognized by many writers (HELLNER, among others), though it is considered as very rare.

We do not know what causes a giant cell tumor to become malignant. W. B. COLEY, who believes that it is a genuine neoplasm, which in about 15 per cent of cases becomes malignant, has pointed out that the malignant mostly are those that have been subjected to postoperative radiation treatment, and he therefore deprecates such treatment, at least as postoperative measure. His material consisted of 23 patients treated by curettage followed by radiation treatment, and of these he states that in 7 cases the tumor became malignant, whereas this was only the case with 1 out of 31 that had been treated only surgically. Of the cases in which radiation treatment had been given, one had been treated with radium, the others with roentgen (dosage not stated). It cannot be seen from the material whether it had been in any way sorted before the choice of therapy was made, and most of the cases related do not seem convincing; so there is really no support for this hypothesis about the effect of postoperative radiation treatment in these cases. The procedure also still has some adherents (HELLNER); but on the whole the tendency in recent years is *to use either roentgen therapy alone* (as first proposed by HERENDEEN) *or surgical therapy;* whereas radium treatment seems to have been abandoned. The roentgen treatment is most often given serially, with fractioned doses considerably smaller than in the case of malignant tumors. SCHINZ and ZUPPINGER for example use doses of 2,400—3,600 r in all These series can be repeated, because *the giant cell tumors, in contrast to the malignant, do not become radioresistent* (LA CHARITÉ). HERENDEEN has called attention to the fact that giant cell tumors in the first month or two after the irradiation show a »*paradoxical reaction*» in the form of passing increase of the tumor and effacement of the bone contours. But after that length of time the reaction subsides, and instead there begins, in the cases where the irradiation has had a favorable effect, a reactive healing process in the form of increased

new formation of bone. American writers, especially, still recommend surgical treatment, however; mostly curettage, because they consider the results of irradiation as uncertain (GESCHICKTER & COPELAND). In this connection it may be mentioned that localized osteitis fibrosa nearly always is treated by curettage. In many cases this lesion subsides spontaneously, though; and, besides, an osteitis fibrosa is, on account of its histologic structure, very little radiosensitive. Epulis gingivae, which is always benign, seems to respond well both to roentgen and radium therapy (KJELLBERG) and to excision.

When a giant cell tumor has become malignant (or in a wrongly interpreted case of osteogenic sarcoma), radical operation is indicated unless there are distant metastases. These tumors are never radiosensitive.

In Denmark, only a few authors have written about giant cell tumors (FLEMMING MØLLER, FLEISCHER-HANSEN et al.), and no case of malignant transformation has been reported. COLLIN has recorded the cure of 10 cases of epulis by radium treatment; all recurrences after surgical operation. Besides, KREBS has reported the cure of 4 epiphyseal giant cell tumors by large doses of roentgen; most of them, though, with resulting ankylosis and destruction of the epiphysis.

As these lesions are very rare (the Mayo Clinic, for instance, has only 3 or 4 cases each year), I have thought it of interest, though the material is small, to *report the cases from the Radium Center in Copenhagen and the surgical service of the Finsen Institute.* All the cases from the period 1930 to 1943 are included, after elimination of a number not sufficiently examined. Of the 47 remaining, 43 were examined microscopically, and nearly all these preparations I have had an opportunity to study; in cases of doubt they have been submitted to Prof. J. ENGELBRETH-HOLM, M. D.

Where there has been doubt about the differential diagnosis between giant cell tumor and osteitis fibrosa in the long tubular bones I have rested my judgment on the clinical picture and the result of the roentgenographic examination rather than on the microscopy, which in these cases often is somewhat inconclusive, because the histologic picture of these lesions no doubt changes somewhat in the course of the disease and especially seems to depend on whether the microscopic examination has been made during the progressive or the regressive phase.

The material is no doubt to some extent a selected one, most of the cases having been referred to the Radium Center and the Finsen Institute from other hospitals; and a number of them are recurrences after previous treatment elsewhere. Though epiphyseal giant cell tumors are generally stated to occur most frequently in the third decade of life, the average age for the patients with this lesion is in my material 42 years; which

also seems to indicate its being more selected, containing a larger proportion of more serious cases; recurrences and malignant transformation being most often recorded in the older age-classes.

The Material from the Radium Center and the Finsen Institute, 1930—1943

Giant cell tumor in epiphyses of long tubular bones	11
(Probably primary osteogenic sarcoma, mistaken for giant cell tumor	1)
Giant cell tumor in short bones and in soft tissue	3
Localized osteitis fibrosa in long tubular bones	8
Generalized osteitis fibrosa	3
Giant cell tumor in upper jaw	1
Localized osteitis fibrosa in upper jaw	2
Epulis gingivae	19
	47 (+1)

The following is a brief summary of the different case histories.

Giant cell tumor in epiphyses of long tubular bones

Case 1. — K 7772. Commercial agent, aged 52 years. — Typical giant cell tumor in medial condyle of femur, verified by microscopy. Curettage, with insertion of radium, 480 mg/h. Since well, function good, no recurrence; followed for 11 years.

Case 2. — R 11572 (and K 11125). Hous wife, aged 34 years. — Giant cell tumor in medial condyle of femur. Microscopy: giant cell tumor with xanthomatous areas. Roentgen treatment, 150 r x 12, total, 1800 r., without effect. Two years later, curettage with good effect. Since well, no recurrence, but ankylosis of knee joint. Followed for 9 years.

Case 3. — K 10484. Housewife, aged 55 years. — Typical giant cell tumor in lateral condyle of tibia, verified by microscopy. Completely cured after curettage. Followed for $8^1/_2$ years.

Case 4. — R 13902. Farmer, aged 49 years. — Typical giant cell tumor in lateral condyle of tibia, verified by microscopy. Roentgen treatment, 4 series with resp. 800, 900, 900 and 900 r. total, 3,500 r, without effect; wherefore curettage. In the following year, recurrence with perforation to the skin; renewed curettage with good effect. Since well, function fairly good, no further recurrence. Followed 7 years.

Case 5. — K 12427. Bicycle-dealer, aged 59 years. — Typical giant cell tumor in medial condyle of femur, verified by microscopy. Curettage (Holbaek County Hospital); two years later recurrence and renewed curettage. Four years later again recurrence and curettage, this time with good effect. Since well, function fairly good, no further recurrence. Followed for $8^1/_2$ years.

Case 6. — R 16725. Housekeeper, aged 44 years. — Probably giant cell tumor in lateral condyle of tibia (no microscopy). Curettage and intense postoperative roentgen treatment, 10,500 r (Aalborg County Hospital). Five years later suddenly roentgen ulcer, but hardly recurrence; excision and curettage. Microscopy: cicatrix from irradiation (?). As there was no tendency to healing, resection; later amputation of femur. Func-

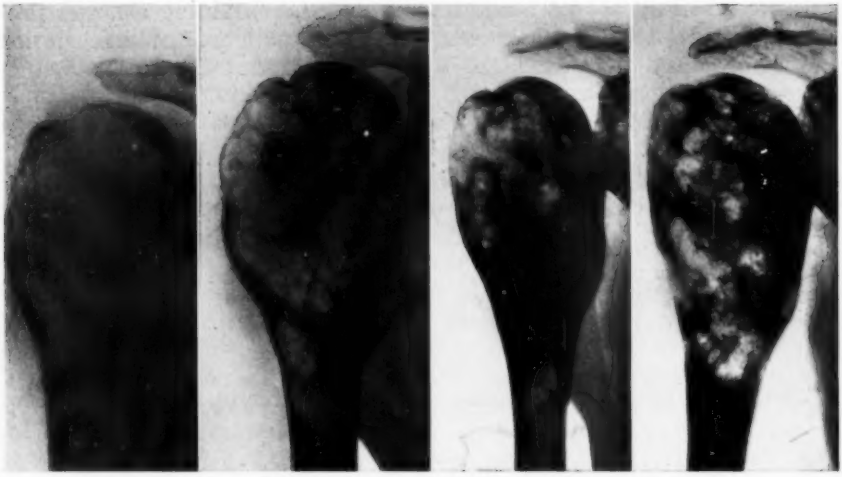


Fig. 1. Fig. 2. Fig. 3. Fig. 4.

Fig. 1. Benign-looking giant cell tumor in head of right humerus untreated. (April, 1940)

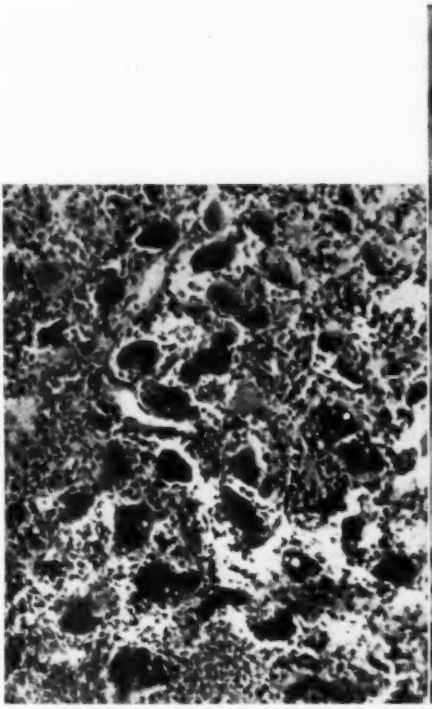
Figs. 2—3. Same tumor after roentgen treatment, resp. 2,400 r (Sep., 1940) and 5,600 r (Oct., 1941). After passing progression, considerable reparatory new bone formations. No signs of malignancy.

Fig. 4. Same tumor, Feb., 1943. In the lower part of the bone there is now considerable destruction with ill-defined limits, large perforation and spontaneous fracture. Strong suspicion of malignant transformation.

tion of stump good. Followed for 6½ years, but only for six months after the amputation.

Case 7. — R 21715. Army officer, aged 28 years. — Clinically and roentgenologically typical giant cell tumor in medial condyle of tibia; *histologically of a type intermediate between giant cell tumor and osteitis fibrosa;* microscopy (twice) showing numerous large and small cysts with hemorrhages and blood pigment. In the walls of the cysts, many giant cells in a rather fibrillar stroma, peripherally, osteoid tissue. Roentgen treatment, 5 series: 600, 1100, 900, 900 and 1800 r, 5300 r in all, without effect. Curettage with good effect. Since well, function good, no recurrence. Followed for 4 years.

Case 8. — R 22255. Farmer, aged 20 years. — Formerly well. In 1937, uncomplicated fracture of right forearm; never injury to right shoulder. In January, 1940, suddenly pain in the latter while working, and, as pain persisted, referred to the Radium Center in April, same year. *Clinically*, general condition good; corresponding to right shoulder slight tumefaction, tenderness and restriction of movement; otherwise nothing objectively abnormal. *Roentgen examination* showed in head of right humerus a benign-looking giant cell tumor, the size of a duck's egg, occupying the whole of the epi- and metaphysis and extending for some distance into the shaft. It was delimited by a thin shell of bone without sure signs of perforation. No spiculae or other signs of malignancy (see Fig. 1).



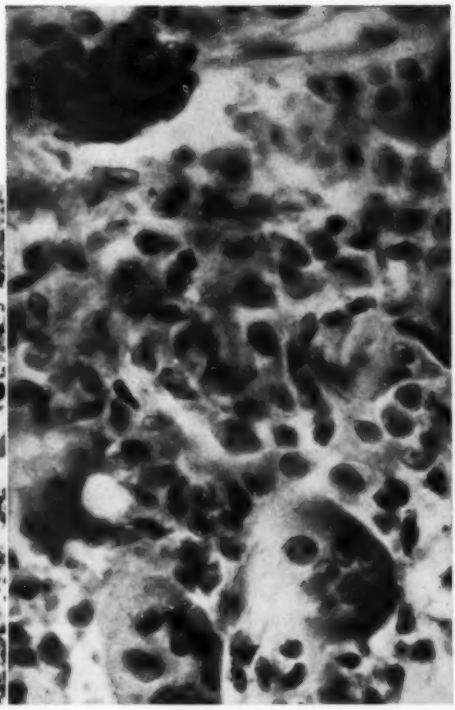


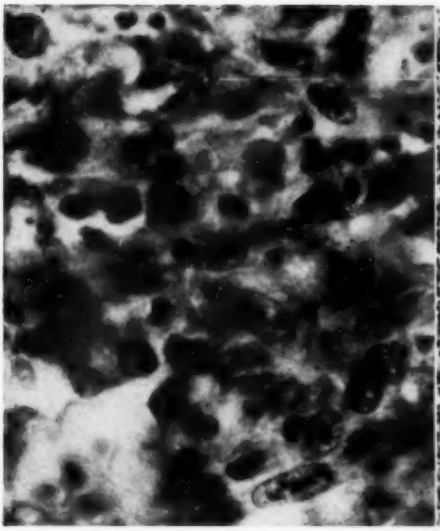
Fig. 5. Fig. 6.

Fig. 5. Biopsy specimen from head of humerus, April, 1940: Untreated, benign-looking giant cell tumor with multinuclear giant cells in typical, non-compacted, slightly fibrillar stroma with copious hemorrhage but no osteoid tissue and no signs of malignancy. (×96),

Fig. 6. Same preparation more highly magnified. No signs of malignancy. (×480).

Biopsy specimen taken with Christiansen's trephine, April, 1940: Rather thick column of tissue, about 1.5 cm. long, consisting of tumor tissue with numerous giant cells with many centrally situated nuclei in a typical, in places slightly fibrillar stroma with ovoid to spindle-shaped, often somewhat angular nuclei. A few, not tumorous mitotic figures, no cellular atypism and no invasive growth in the surrounding adipose tissue. Copious hemorrhage and a little bone tissue in the process of resorption, but no osteoid tissue. Histologic diagnosis: Benign-looking giant cell tumor. (Figs. 5 and 6.)

The patient was given *roentgen treatment* from April, 1940, to May, 1942, 6 series in all, of resp. 800, 1600, 800, 1200, 1200 and 800 r; total, 6400 r (180 kv.; 0.5 mm. Cu.; distance. 40 cm.; field, from 10×15 to 20×24 cm; 100—200 r per dose). Several controlling roentgen examinations showed in the beginning some progression of the tumor, later continued healing with considerable reparatory new bone formation both in the compacta and in the many sharply delimited trabeculae. No signs of malignancy. (Figs.



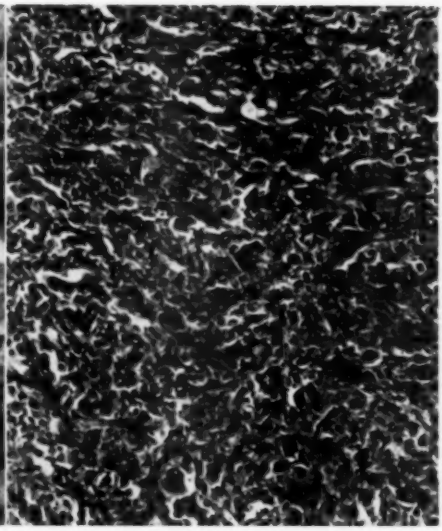


Fig. 7. Fig. 8.

Fig. 7. Tissue removed by curettage March, 1943: heaps of large cells, suspected to be sarcoma cells; with irregular, in many cases enormous nuclei with tumor-like mitotic figures.

Fig. 8. April, 1943: Polymorphocellular (osteogenic) sarcoma with close-set, mostly spindle-shaped cells with some fibril formation, enormously varied nuclei and abnormal mitotic figures.

2 and 3.) Also the subjective symptoms disappeared, and from May, 1942, the patient was in possession of his full capacity for work, with only a slight restriction of movement in the right shoulder joint. During this time no microscopic examination was made.

In January 1943, — that is about 3 years after the affection began, — he suddenly, while working, again felt a pain in his right shoulder. In February there was considerable restriction of movement, and a *roentgen examination* now showed in the lower part of the former giant cell tumor, over an area about the size of a tangerine, considerably increased destruction, with numerous vaguely delimited rarefactions; and, laterally, a large perforation and spontaneous fracture. Malignant transformation was strongly suspected (Fig. 4). *Biopsy* (Feb., 1943) showed necrotic tissue with infection. Here and there in the tissue there were a few heaps of cells, rather suspected to be sarcoma cells, with large, irregularly shaped, in some cases enormous, nuclei; but of the original giant-cell tumor tissue nothing was seen.

The patient was febrile, but his general condition otherwise good. As it was taken for granted that giant cell tumors always are benign, the changes were interpreted as being due to the spontaneous fracture, and the case for a time merely kept under observation. In March, 1943, *curettage* was performed. The *microscopy*, as the last time, concluded in: sarcoma suspected (Fig. 7). But the general condition gradually became affected, and renewed *biopsy* from the tumor now showed indubitable polymorphocel-

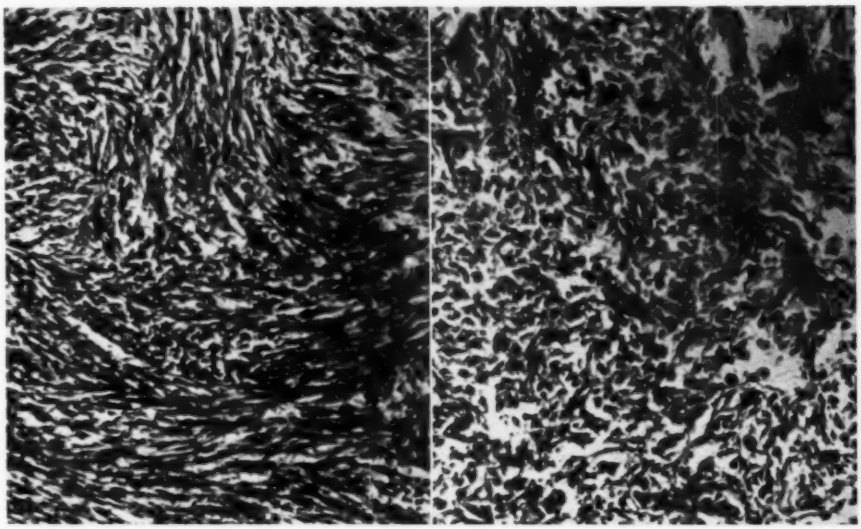


Fig. 9. Fig. 10.

Fig. 9. May, 1943: Tissue from the amputated tumor. Marked fibril formation and many mitotic figures.

Fig. 10. May, 1943: Another portion of the same tumor, with marked nuclear polymorphism.

lular (osteogenic[1]) sarcoma with numerous, mostly spindle-shaped, cells, lying close to each other, with greatly varied, enormously hyperchromatic nuclei and numerous abnormal mitotic figures. There was moderate fibrillation, but no osteoid tissue. (Fig. 8.)

In May, 1943, *interthoracoscapular amputation* was done, chiefly as palliative measure. Corresponding to the head of the humerus there was found a tumor, as large as the head of a child, filling the entire marrow cavity of the caput humeri, of which there remained only a thin shell, with invasion into the soft tissues on all sides; besides considerable inflammation with several abscesses. The joint was intact. *Microscopy*, both from the marrow cavity and from the masses of tumor in the muscles showed, as before, polymorphocellular (osteogenic) sarcoma. Large portions of the tumor tissue was built up of close-set fusiform cells with marked fibril formation (Fig. 9); in other places, polymorphous oval or round cell nuclei dominated (Fig. 10). Everywhere considerable cellular atypism and numerous tumor-like mitotic figures; besides, considerable infection in the tumor; but no giant cells or osteoid tissue.

In June, same year, *roentgen examination* at the Radium Center showed metastasis in the right lung, and in September, same year, it was reported from the hospital in Svaneke that the metastases had grown larger and were now giving marked symptoms, and enormous recurrences of the tumor had developed in the cicatrix from the

[1] The term osteogenic sarcoma is here everywhere used in the sense in which it was first used by EWING, of a malign bone tumor arisen from cells with the potential power of bone formation (CUTLER & BUSCHKE).

operation. *Microscopy* from one of these metastases (which was as large as a man's head) showed polymorphocellular sarcoma, exactly as before. The patient died in September, 1943, in a state of extreme cachexia, $3^1/_2$ years after the onset of the disease. Necropsy was not performed.

Epicrisis. — A farmer, aged 20 years, with a clinically, roentgenologically and histologically typical, benign-looking giant cell tumor in the head of the humerus was treated by roentgen irradiation 6 times in the course of 2 years, being given, in all, 6500 r, with good subjective effect and marked roentgenologic signs of healing. Three years after the onset of the disease, the condition suddenly got worse, with spontaneous fracture; and markedly malignant, osteogenic sarcoma was ascertained, which despite amputation led to enormous metastases in the cicatrix from the operation and clinical and roentgenologic signs of metastases in the lungs. Death supervened 9 months later.

Discussion. — The case seems to be a clear one of malignant transformation of a benign cell tumor into an osteogenic sarcoma. The only possibility of error is that there in some other part of the original tumor may have been sarcomatous portions which had not been reached in the trephining for biopsy sample. If that is the case, the growth would have been a primary sarcoma that had masked itself as a benign giant cell tumor — or a malignant giant cell tumor. Despite the rather large column of tissue from the trephining deep into the tumor, this possibility cannot be excluded, of course. Like the cases from the literature, this case can therefore at most be taken as support for the *probability* of giant cell tumors being capable of malignant transformation. For the clinician, this is, however of minor importance. The principle is the ascertainment of *the fact that a to all appearances benign giant cell tumor may eventually end as a malignant sarcoma*, which means *that it is impossible to be absolutely sure that an observed giant cell tumor may not become malignant*, though such a transformation undoubtedly is rare. I am inclined to believe that it would be very rare if a thorough examination were always made at once *of the whole tumor* — that is if curettage were always done to begin with; because thus the suspect cases would be eliminated.

Case 9. — R 27399. Workingman, aged 33 years. — Typical giant cell tumor in the head and neck of the radius, verified by microscopy. Roentgen treatment: 2 series, each of 3,000 r; 6,000 r in all; without sure effect. Followed for 16 months.

Case 10. — R 30120. Housewife, aged 47 years. — Typical giant cell tumor in lateral condyle of tibia, verified by microscopy. Roentgen treatment: 3 series, of resp. 1,000, 800 and 1,500 r; total, 3,300 r, without sure effect. Followed for 1 year.

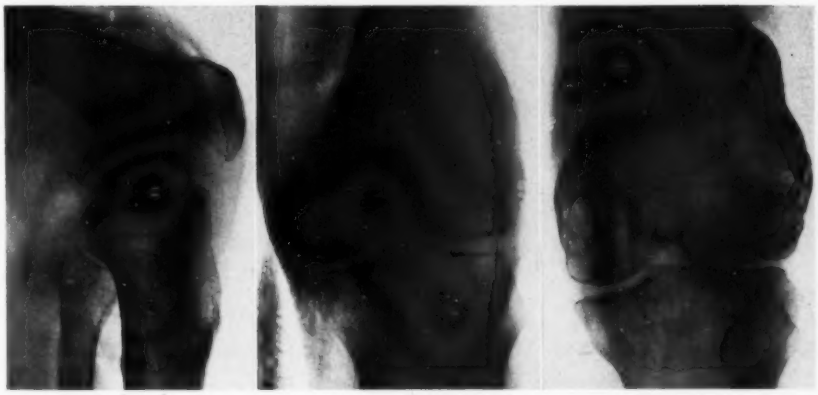


Fig. 11. Fig. 12. Fig. 13.

Figs. 11—12. Lateral and anterior views of right knee, untreated; Oct., 1935: Finely lobulated, orange-sized tumor in lateral condyle of right femur; some suspicion of malignancy, but not unlike a giant cell tumor.

Fig. 13. Same tumor, Oct. 1938, (3 years after intensive roentgen treatment): Marked consolidation of the compact tissue and the trabeculae more sharply defined. The growth now most nearly resembles a giant cell tumor in the process of healing.

Case 11. — R 31002. Housewife, aged 47 years. — Typical giant cell tumor in distal epiphysis of radius, verified by microscopy. Roentgen treatment; 1 series, 600 r, in all; without effect. Later, curettage, with good effect. Followed for 18 months.

To show what difficulties the differential diagnosis sometimes may present, I relate the following case, in which the tumor, from which the patient eventually died, for several years resembled a giant cell tumor.

Case 12. — K 17546. Coal merchant, aged 51 years. — Formerly well. Had for two years been complaining of pain in the right knee. No preceding trauma, but during the course of the disease several severe injuries. In October, 1935, *roentgen examination* showed in the right lateral condyle of the femur a tumor, the size of an orange, occupying the whole epi- and metaphysis and extending for some distance up into the shaft. The bone, which was somewhat puffed up, was by the very finely lobulated tumor reduced to a paper-thin shell. The delimitation upwards toward the sound bone tissue was a little vague, but there were no spiculae. There was some suspicion of the tumor being malignant, but it rather resembled a giant cell tumor (Figs. 11—12). He was in the course of 5 months, without preceding biopsy, given fractioned *roentgen treatment*, 200 r×50; total, 10,000 r, to the right knee, with good effect on the pain; the condition otherwise unchanged.

In October, 1938, recurrence; and he was admitted to the Copenhagen County Hospital, Gentofte, Service H, where *roentgen examination* showed that the tumor had progressed a little, but now showed marked consolidation both of the compact tissue and of the trabeculae, with sharp delimitations; it now most nearly resembled a giant cell tu-

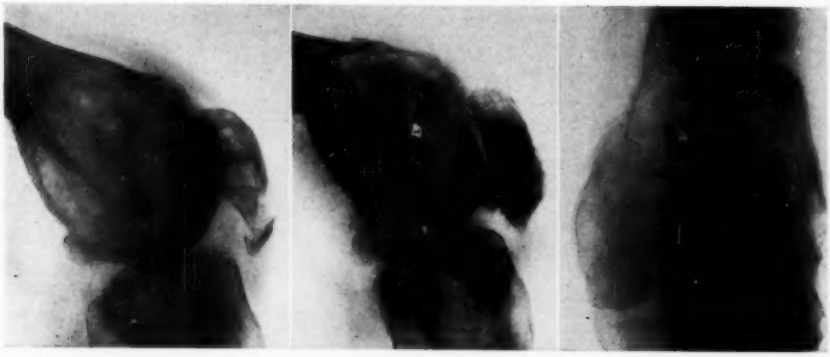


Fig. 14. Fig. 15. Fig. 16.

Fig. 14. Same tumor July, 1940: Further consolidation of the compact tissue, indicating continued progress of the process of healing. Besides, several strain fractures, but no signs of malignancy.

Figs. 15—16. Jan. 1941: Now unmistakable osteogenic sarcoma with effaced structure and large massive, cotton-woolly shadows.

mor in the process of healing (Fig. 13). *Curettage* was done, and masses of yellowish-white granulation tissue removed. *Microscopy:* osteitis (? osteitis fibrosa).

In 1940, there again came recurrence, and the patient was referred to the surgical service of the Finsen Institute, where *roentgen examination* (July, 1940) as before showed giant cell tumor, but now with a little better consolidation as expression for further healing. Besides, there were several strain fractures around the knee-joint; thus, in the patella; but no signs of malignancy (Fig. 14). The case was still considered as a giant cell tumor, and the patient was kept under observation, but no biopsy was performed.

In January, 1941, the pain became more intense, the knee became very much swollen, there were hard, prune-sized lymph nodes in the right crural region, and also the general condition was visibly affected. *Roentgen examination* now, — seven years after the onset of the disease, — showed an entirely different picture. The tumorously rarefied area had become larger, and the structure was very much effaced. In the distal half of the patella and in both femoral condyles there were considerable, massive, cotton-woolly shadows, as expression for new bone formation, and the interarticular space was almost entirely effaced. The picture was now clearly that of a sarcoma (Figs. 15—16). *Trial boring* from the tumor (Jan. 1941) showed unmistakable polymorphocellular (osteogenic) sarcoma with tissue rich in fibroblasts, marked cellular atypism, hyperchromatic nuclei and abnormal mitotic figures; but no osteoid or cartilaginous tissue, and no giant-cell tumor tissue (Fig. 18). After *preoperative irradiation* with roentgen (100 r × 10; total, 1,000 r), palliative high *amputation of femur*, with excision of the lymph nodes, was performed.

After the amputation, the patient went rapidly downhill, got pains in the abdomen and hemoptyses; and in August, 1941, he died at home, about eight years after the onset of the disease.

The *microscopy* from the curettage at the County Hospital in Gentofte, in 1938, was now revised. The tumor consisted for the greater part of highly fibrous tissue poor

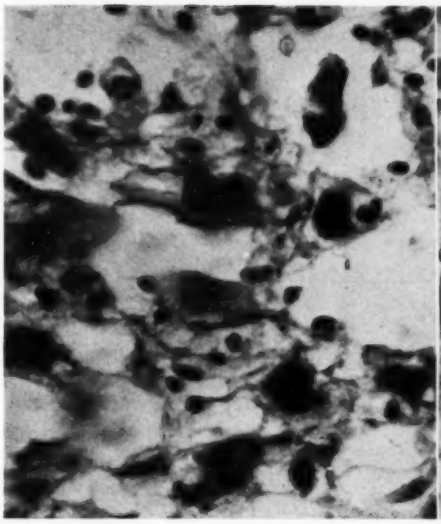


Fig. 17.

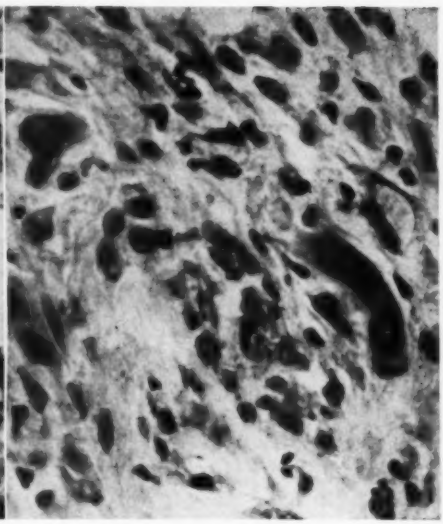


Fig. 18.

Fig. 17. Tissue from curettage Oct., 1938: Loose tissue with polymorphous tumor-like cells with enormous irregular nuclei and large nucleoles; besides, a few mitotic figures and double nuclei, but no giant cells. Sarcoma, probably osteogenic.

Fig. 18. Biopsy specimen from tumor, Jan., 1941: indubitable polymorphocellular sarcoma (osteogenic); tissue rich in fibroblasts, with marked cellular atypism, hyperchromatic nuclei and abnormal mitotic figures.

in cells, which in some places was necrotic. In other places there were scattered hemorrhages, and, besides, there was some myxomatous tissue. In a few places there were areas with numerous polymorphous, tumor-like cells, some of them with large, irregular nuclei and large nucleoles, here and there double nuclei and a few mitotic figures; but no giant cells. There was no cartilaginous or osseous tissue, and no cysts (Fig. 17). On account of the tumor-like elements, *the tumor must be considered as having already at that time been a sarcoma, probably osteogenic.* The dominating fibrous portions may have been expression for a cicatrix from the intense irradiation three years previously.

Discussion. — Unfortunately no biopsy was made at the first treatment, in 1935, and the case is therefore not quite clear. From the microscopies it appears that the patient in all probability already at the time of the first recurrence, in 1938, has a sarcoma, though a slightly malignant one, but there is nothing in the microscopy to indicate that this sarcoma should have developed from a giant cell tumor; though this does not exclude the possibility that such may have been the case. Nor yet are the roentgenograms quite typical, since there at the first examina-

tion was some suspicion of malignancy whereas the later roentgenograms, on the contrary, pointed rather to a benign giant cell tumor in the process of healing. No doubt the patient in 1941 had a slightly malignant sarcoma, which eventuated in death. I should think it *most probable* that the tumor in this case has been *an originally only slightly malignant, osteogenic sarcoma, which for seven years has masked itself as a benign giant cell tumor and in that time gradually has become highly malignant.*

The case shows the necessity ot careful and repeated examination in all doubtful cases, and especially the necessity, in all cases, of immediate biopsy.

We thus have here *11 cases of epiphyseal giant cell tumors in long tubular bones*; Case 12 not being included. All except Case 6 were verified histologically. Six of the eleven were followed for over five years, two for over three years. *Of these 8, one (Case 8) became malignant and eventuated in death from osteogenic sarcoma.* Of course, conclusions respecting the frequency of malignant transformation of giant cell tumors on the basis of a numerically so small, and, moreover, selected, material are not warranted. Also Case 7 is interesting, histologically, as seeming to show *a transitional form between giant cell tumor and osteitis fibrosa.*

On the whole, the material corresponds well to the large compiled materials from America, but it is curious to note that though trauma is generally considered as an important factor for the development of these tumors, there was trauma in the anamnesis of only three, or, at most, four of our cases.

The roentgen treatment was in most of the cases given in several series, with intervals of some months between each; and each series fractioned, with daily doses of from 100 to 200 r. The doses were, however, considerably smaller than »cancer doses»; in most cases 800 to 1,200 r in each series; the maximum 1,800 r (180 kv.; 0.5 mm. Cu.; distance, 40 cm.; and rather small fields).

In 7 of the cases, roentgen treatment was given as the first therapeutic measure; but only in one case (Case 8) a positive favorable effect was observed, and this eventually showed malignant transformation. *In none of the cases observed for a longer period than 18 months after the roentgen treatment subsequent operation was avoided.* The material thus speaks against the efficiency of the roentgen treatment; but it must not be forgotten that the material probably is rather selected. As this therapy has given excellent results elsewhere, the services do not think of abandoning it, but will continue to use it, only with the employment of somewhat higher doses.

Giant cell tumor in short bones and soft tissues

Case 13. — R 23612. Boardinghouse keeper, aged 30 years. — Giant cell tumor in the talus, verified by microscopy. Curettage (Nykjoebing Sj. Hospital). Twelve years later, recurrence and again curettage, followed by roentgen treatment: 2 series, each of 600 r; total 1,200 r; with good effect. Since well, function good, no recurrence. Followed for 3 years after last operation.

Case 14. — K 11892. Domestic servant, aged 20 years. — Hazelnut-sized giant cell tumor in soft tissue radially to first phalanx of 3rd finger, verified by microscopy. Cured after extirpation. Followed for 5 years.

Case 15. — K 11975. Housewife, aged 50 years. — Bean-sized giant cell tumor adhering to extensor tendon of 5th finger, at level of ungual phalanx; verified by microscopy. Extirpation. No follow-up.

The microscopy showed in all three cases numerous giant cells in coarsely fibrous tissue, with many centrally situated nuclei. There were no signs of infection. The location of the two cases in the fingers makes it very likely that they may have arisen from sesamoid bones.

Localized osteitis fibrosa in long tubular bones

Case 16. — K 6543. Tobacconist, aged 34 years. — Probable bone cyst in medial malleolus. Roentgenologic diagnosis: ? osteitis; ? cyst. Microscopy: detritus-filled multilocular bone cyst with connective tissue walls and hemorrhage; but no giant cells or signs of infection. Complete cure after curettage. Followed for 7 years.

Case 17. — K 10284. Girl, aged 14 years. — Localized osteitis fibrosa in shaft of tibia. Microscopy: A few small giant cells in fibrillar stroma with osteoid tissue and bone in the process of resorption, but no cysts or hemorrhage. Roentgen treatment 4×5 Sabouraud (Bispebjerg Hospital, service A), with some effect. Five years later, spontaneous fracture, curettage, recurrence and renewed curettage, this time with good effect. Since well, function good, no further recurrences. Followed for 15 years; 6 years after the last operation.

Case 18. — K 11765. Nurseryman's apprentice, aged 16 years. — *Typical gigantocellular epulis gingivae + bone cyst in shaft of tibia* (of the latter, no microscopy). Serum calcium, normal. Serum phosphorus, 5—8 mg per cent. The epulis treated by curettage (Copenhagen County Hospital, Frederiksberg), postoperative roentgen treatment: total, 4,100 r, with good effect. Four years later, the cyst in the tibia spontaneously regressed. Since well, function good. Followed for 7 years.

Case 19. — K 12392. Girl, aged 1 year. — *Polycystic osteitis fibrosa in shafts of tibia and fibula*, verified by several microscopies. Serum calcium and -phophorus, normal values (several tests). Curettage, twice, of both bones; later, in spite of repeated operations, pseudarthrosis, but hardly recurrence. Followed for 7 years.

Case 20. — K 12404. Domestic servant, aged 22 years. — Clinically and roentgenologically, bone cyst in shaft of tibia; *histologically, type intermediate between giant cell tumor and osteitis fibrosa;* the microscopy showing a large, solid tumor with numerous typical multinuclear giant cells in a highly fibrillar stroma of fusiform cells, with copious hemorrhage, but no cysts or osteoid tissue. The histologic picture resembles the »spindle cell variant of giant cell tumor» described by GESCHICKTER & COPELAND. — Curettage (Aalborg County Hospital). There is still a fistula; but otherwise the patient is symptom-free, with good function. Followed for 9 years.

Case 21. — R 16497. Boy, aged 10 years. — Typical bone cyst in lower part of shaft of tibia, verified by microscopy. Spontaneous fracture. Curettage. Since well, function good, no recurrence. Followed for 5 years.

Case 22. — R 18601. Girl, aged 18 months. — Clinically and roentgenologically, bone cyst in upper part of shaft of humerus, with spontaneous fracture. No microscopy. Complete spontaneous healing. Followed for $5^1/_2$ years.

Case 23. — R 27143. Boy, aged 15 years. — Bone cyst, the size of a duck's egg, in upper part of shaft of humerus; verified by two microscopies. No histologic signs of malignancy. As the tumor progressed rapidly, primary resection was done, with transplantation of bridge from the fibula. Since well, function fairly good, no recurrence, but only followed for 15 months.

We thus have, in all, 8 fairly sure cases of localized osteitis fibrosa in long tubular bones; for two of which there is, however, no microscopic verification. None of the cases became malignant. In Case 18 there was a combination of epulis gingivae and bone cyst in the tibia. The serum calcium values were normal, but the serum phosphorus repeatedly increased. In Case 19 there were cysts both in the tibia and in the fibula, but the blood values were normal. Another interesting case is no. 20, which showed a type histologically intermediate between giant cell tumor and osteitis fibrosa. The material furnishes a good illustration of *the variegated picture of these lesions* and the difficulties which the differential diagnosis often presents both for the clinician and for the histologist.

Generalized osteitis fibrosa

The material contained 3 cases (nos. 24, 25 and 26) of *generalized osteitis fibrosa*, of which only the first is verified histologically, however; (it has formerly been published by O. CHIEVITZ & H. C. OLSEN). In two of the cases there were multiple cysts, in the third only general halisteresis with spontaneous fractures; in none of them there were giant cell tumors. In two of them there was renal calculus. In all of them, there were typical hematologic changes, and they were cured after removal of a parathyroid adenoma. The cases have been followed up for respectively 11, $2^1/_2$ and 8 years after the operation.

Giant cell tumor and osteitis fibrosa localized to bones of the head, inclusive epulis gingivae

Finally, I shall relate the cases *localized to bones of the head*, 22 in all; of which 3 were located in the upper jaw, while the others were cases of epulis gingivae.

Case 27. — R 8604. Housewife, aged 44 years. — *Giant cell tumor in the left maxilla*, with extensive destruction in the premolar region of the alveolar process, later also in the hard palate and the maxillary sinus. Microscopy: numerous giant cells in a moderately fibrillar stroma with chiefly spindle-shaped cells, but no bone- or cyst formation. *The tumor had perhaps arisen from an epulis gingivae.* Roentgen treatment: 2 series of resp. 2,400 and 3,200 r, total, 5,600 r, without effect; therefore curettage and insertion of radium, 1,350 mc/h. Microscopy now showed fewer giant cells and markedly fibrillar stroma (? radiation effect). Good effect of the operation and the radium treatment. No recurrence. Patient died from other cause, 10 years after the operation.

Case 28. — K 12023. Boy, aged 8 years. — *Benign tumor of left maxilla, probably osteitis fibrosa. Not arisen from any epulis.* By operation, a large, solid, firmly fibred, reddish brown tumor was extirpated, which had invaded the maxillary sinus, whereas the alveolar process was not involved. Microscopy showed an essentially fibrillar connective tissue with abundant collagenic, partly hyalinized fibrils and a quantity of osteoid tissue; besides, there were a few scattered heaps of large multinuclear typical giant cells and some little hemorrhage; but no cysts or signs of malignancy. The microscopic picture most resembled that of an osteitis fibrosa. The patient has since been well, there has not been any recurrence. Followed for $5^1/_2$ years.

Case 29. — R 33108. Domestic servant, aged 20 years. — *Benign tumor of the right maxilla, probably osteitis fibrosa; hardly arisen from any epulis gingivae.* Operated upon in the Nykjoebing (Falster) Hospital for »a large cyst in right maxillary sinus with progression to the sphenoid and the ethmoid bone; the tumor possibly arisen from the root of a tooth. Microscopy: dental cyst with chronic inflammation». Three years later, recurrence set in and the right maxillary sinus was resected (Copenhagen County Hospital, Gentofte, Service E). The orbital wall seemed to be eroded by the tumor; but, as previously, there were no signs of epulis gingivae. Microscopy: fibrillar stroma with numerous spindle-shaped cells and some osteoid tissue, but only here and there multinuclear giant cells, and no cysts. Copious hemorrhage and blood pigment; no signs of malignancy. The microscopic picture corresponds well to that of osteitis fibrosa. The patient was given postoperative roentgen treatment: total, 4,275 r; which seems to have arrested the growth of the tumor. Followed for $3^1/_2$ years.

Discussion. — Case 27 is perhaps one of the rare ones in which an epulis gingivae invades the bone. Otherwise it nearly always proliferates outwards. No. 28 and no. 29 are interesting, because they *both seem to be cases of localized osteitis fibrosa of the maxilla and at least one of them has no relation to an epulis.* The location is rare; among GESCHICKTER & COPELAND's 22 cases there is not a single one in this site. But, as a rule, these lesions will probably not be diagnosed, but will be called osteofibromas or something similar.

Epulis gingivae

The material consists of 19 cases, all verified histologically. Histologically, they fall into two groups: gigantocellular epulis (17 cases) and fibromatous epulis (2 cases). The angiomatous types, which by some are called angiomatous epulis (epulis being merely a regionally determined designation), are not included. A closer scrutiny of the preparations gives one the impression of *an even, gradual transition* from cases which histologically hardly can be distinguished from epiphyseal giant cell tumors, through the most common form, in which the stroma chiefly consists of spindle-shaped cells with considerably more fibril formation and osteoid tissue, while the giant cells and the hemorrhages become fewer, to cases in which there are no giant cells, but marked fibroostosis; — the type here called fibromatous epulis. Where the line of demarcation should be drawn must, I think, be a matter of opinion. Where it is a question of osteitis fibrosa, the histology is, in fact, quite uncertain. *Few diagnoses have probably in the course of time been so misused as this, which does not cover any precise, well defined pathologic field.* Almost any connective tissue reaction in bone has at some time or other been designated by that term. Too superficial biopsy is another source of error. The peripheral portions of a giant cell tumor usually contain a great deal of connective and osteoid tissue, but no giant cells; on the basis of such a preparation one is easily led to diagnose the case as osteitis fibrosa, whereas a later microscopy may show unmistakable giant cell tumor.

The age of the patients varied from 7 to 69 years; only three were under 20 years old. Roentgen examination showed in about half of the cases rarefactions corresponding to the alveole; in none of them there was invasion of any deeper seated bone. All the cases were followed for over 3 years, nine were observed for over 5 years. In none of the cases malignant transformation occurred (such transformation has never been observed). They all became entirely symptom-free, most of them after the first treatment; a few, however, were recurrent cases from other hospitals. Ten of them were treated surgically, by extirpation or excision with or without electrocoagulation of the base, one was a recurrence after operation elsewhere. Exclusive roentgen therapy was employed in 4 cases, two of them recurrences after surgical operation. The treatment was in most of them given as close irradiation in doses of 300 to 500 r. daily, total, 2,000. 3,000 to 5,000 r; with 60 kv., 4 ma. Combined surgical and roentgenologic treatment was used in 5 cases. Radium was not employed.

All the methods of treatment employed have given good results in this absolutely benign affection. I wish to stress this, because the advocates

of roentgen treatment of giant cell tumors emphasize the excellent effect in the treatment of epulis and on that basis often uncritically extend the same to apply to the far less tractable epiphyseal giant cell tumors in long bones. This is, for instance, the case with LACHARITÉ's report of 14 cases, of which 12 were epulis.

Conclusion

The present material corresponds on the whole fairly well to the large collected materials from the United States of America. *It illustrates the enormously variegated picture which these lesions present*, because it in spite of its numerical smallness contains many forms intermediate between the different groups and thus clearly shows the very near relationship between giant cell tumor and osteitis fibrosa.

My study of the cases, especially the histologic examination, has *not* enabled me to sort out from among the giant cell tumors a group which might be considered as genuine neoplasms, such as JAFFE and his coworkers have believed it to be possible. On the contrary, *there seems to me to be an even, gradual transition to osteitis fibrosa* (which certainly is not a neoplasm). For the same reason *I have not found it expedient to subclassify these tumors, of which by far the greatest part are benign, into different grades.*

The material does not tell us anything about the nature of the so-called malignant giant cell tumors. *Only one case* (no. 8) *underwent malignant transformation into an osteogenic sarcoma*, and in this case the original microscopy consisted only in examination of a specimen obtained by trephine biopsy, which showed benign-looking giant cell tumor. Thus, the possibility cannot be excluded that microscopy of the whole tumor would have shown malignant giant cell tumor (or osteogenic sarcoma). A couple of similar cases, with lethal isssue, one of which (no. 12) is related, proved on closer examination to have probably been primarily malignant, osteogenic sarcomas, which in the beginning had masked themselves as benign giant cell tumors. The same is indeed the case with the great majority, by far, of the cases published as examples of malignant transformation of giant cell tumors; though a few of them seem rather convincing. For the clinician it is important, however, to know *that an osteogenic sarcoma in the beginning not infrequently may to the point of deception resemble a benign giant cell tumor, and particularly that the roentgenologic pictures of the two conditions may be exactly alike; so that the possibility of the case being an osteogenic sarcoma cannot be excluded with certainty except on the basis of a histologic examination.* I also wish to emphasize that although a giant cell tumor in the overwhelming majority of cases will remain benign, *there is no absolute certainty that*

it may not eventually become malignant. In doubtful cases, — and among such are especially recurrences affecting the general condition and cases where the patient is in an advanced age, — renewed biopsy and revision of the original microscopy are therefore advised. On the other hand it is just as important that no unnecessary, mutilating measures are resorted to in these for the overwhelming part benign affections. Therefore, it must be remembered that their appearance when they recur, and especially if they have become infected or have been subjected to roentgen treatment, in most cases changes considerably; but that this does not mean that they have become more malignant.

The etiology and pathogenesis of these affections are still obscure; especially are biochemical and histologic examinations lacking. The present material gives no information in these respects, beyond the fact that none of the 47 cases either as regards the age of the patients or the site of the lesions are contrary to GESCHICKTER & COPELAND's theory, according to which they are an abnormal phase of the growth of bones preformed in cartilage, or of the deciduous teeth. It is worthy of note, though, that trauma was rare in the anamnesis of these cases, while American authors ascribe considerable importance precisely to preceding injury as determining factor.

In conclusion, I shall briefly touch on a few important questions respecting these lesions from the clinical point of view.

The giant cell tumors in the epiphyses of long tubular bones can be more or less defined by comparison of the clinical, roentgenologic and histologic findings, and can thus be distinguished from the forms localized to the meta- or diaphyses and termed localized osteitis fibrosa. In most cases, the latter consists in a solitary bone cyst; but sometimes the affection is polycystic, mostly in the same bone, more rarely in several. In short and flat bones, in facial bones preformed in cartilage, and along the border of the jaws, cysts are found which histologically mostly show forms intermediate between giant cell tumor and osteitis fibrosa. In all these cases, the serum calcium and serum phosphorus levels are normal, in contrast to what is the case in generalized osteitis fibrosa, which mostly (or always) is determined by a parathyroid adenoma and is cured by the removal of the latter. Since the last-named affection may begin as a giant cell tumor, a local bone cyst or an epulis, it is advisable always to make a serum calcium and -phosphorus analysis.

In all cases, the question between benign and malignant must be decided by a combination of all diagnostic aids; especially must the possibility of osteogenic sarcoma be considered. The disease is in the overwhelming majority of cases benign, though recurrence is frequent and the course mostly year-long. In epiphyseal giant cell tumor, the func-

tion of the joint is often compromised, even after healing; and on the whole this type is considerably more obstinate. It is also here that the possibility of malignant transformation must especially be borne in mind.

Before the treatment is instituted, biopsy should always be performed, either by excision or by means of trephine. Biopsy has formerly been hesitated from especially in the case of bone tumors, for fear of causing increased spread of the tumor cells. This fear seems to be groundless, though; and that metastasising should increase after biopsy has never been proved (ENGELBRETH-HOLM).

The treatment varies according to the site of the lesion and the other conditions in the individual case. The epiphyseal giant cell tumors are mostly treated either by curettage or by irradiation with roentgen. At present it is impossible to say which of the two methods is the best. In most cases I would myself prefer curettage also for the reason that it gives possibility for microscopy of the whole tumor, whereby one is enabled to recognize at once any possible existing malignant characters of an otherwise benign-looking growth. The combination of surgical operation and radiation therapy is by many deprecated as inefficacious or directly dangerous. At any rate it offers no advantages. In suspicious cases there may be question of resection or amputation. In case of osteogenic sarcoma radical operation is the only chance. In case of recurrence, the treatment may be repeated; but for the most part operation will be preferable; in obstinate cases perhaps resection.

It is difficult to give definite indications for the manner in which the roentgen treatment should be given. It is generally agreed, though, that the doses (given fractioned) should be considerably smaller than in cancer, and that any considerably cutaneous reaction should be avoided, so that the treatment may be repeated several times at intervals of a few months. Radium therapy seems to be of little effect.

Localized osteitis fibrosa is best treated by curettage; but there are many latent or slightly symptom-giving forms whose tendency to spontaneous healing renders treatment superfluous. If there is spontaneous fracture, bandaging in the usual manner will mostly be sufficient. In the cases which histologically resemble giant cell tumor, roentgen treatment may be tried, but is otherwise of little effect.

The numerous intermediate forms, for instance in vertebrae, ribs, pelvic or cranial bones, often have a considerable tendency to spontaneous healing. In many of these cases roentgen treatment will be preferred to the often risky and technically difficult operations in these regions. Epulis gingivae seems to respond well both to excision, roentgen and radium. In cases of generalized osteitis fibrosa, examination should be made for parathyroid tumor. The tumor can very rarely be palpated

in the neck; even if the objective finding is negative, operation should therefore be proceded to if there are typical hematologic changes. When the adenoma responsible for the condition is removed, the bone cysts usually regress spontaneously.

All in all, giant cell tumor and osteitis fibrosa are, despite the many unsolved problems, fields in which treatment is well repaid.

SUMMARY

The author reports 47 cases of giant cell tumor and osteitis fibrosa from the Radium Center in Copenhagen and the surgical service of the Finsen Institute. A case of clinically, roentgenologically and histologically benign-looking giant cell tumor in the head of humerus became 3 years after roentgen treatment transformed into an osteogenic sarcoma with lethal issue. A probably primarily malignant, osteogenic sarcoma in the condyle of femur, after masking itself for 7 years as benign giant cell tumor, led to the patient's death from osteogenic sarcoma. In contrast to curettage, roentgen therapy was found of little effect in epiphyseal giant cell tumors. Histologic scrutiny showed an even, gradual transition between giant cell tumor and localized osteitis fibrosa, and it was not found possible to subclassify these tumors into different grades.

ZUSAMMENFASSUNG

Verf. berichtet über 47 Fälle von Riesenzellentumor und Osteitis fibrosa aus der Radiumzentrale in Kopenhagen und der chirurgischen Abteilung des Finseninstituts. Ein Fall von klinisch, röntgenologisch und histologisch gutartig aussehendem Riesenzellentumor des Humeruskopfes ging 3 Jahre nach Röntgenbehandlung in ein osteogenes Sarkom mit tödlichem Ausgang über. Ein wahrscheinlich primär malignes, osteogenes Sarkom im Femurkondylus führte, nachdem es sich 7 Jahre lang unter der Maske eines gutartigen Riezenzellentumors verborgen hatte, zum Tode des Kranken an osteogenem Sarkom. Zum Unterschied von Auskratzung erwies sich Röntgenbehandlung bei Riesenzellentumoren der Epiphysen als wenig wirksam. Histologische Untersuchung ergab schrittweise alle Übergänge zwischen Riesenzellentumor und lokalisierter Osteitis fibrosa, und es gelang nicht, bei diesen Tumoren je nach dem verschiedenen Grade Unterabteilungen zu unterscheiden.

RÉSUMÉ

L'auteur relate 47 cas de tumeurs à cellules géantes et d'ostéite fibreuse provenant du Centre radiothérapique de Copenhague et du Service chirurgical de l'Institut Finsen. Un cas de tumeur à cellules géantes d'aspect bénin tant du point de vue clinique et radiologique qu'histologique, dans la tête de l'humérus, se transforma trois ans aprés un traitement aux rayons de roentgen en un sarcome ostéogénique avec terminaison mortelle. Un sarcome ostéogénique du condyle du fémur, de caractère malin probablement dès son début, après s'être masqué sept ans durant sous les apparences d'une tumeur bénigne à cellules géantes, fut cause de la mort du malade. La thérapeutique par les rayons de roentgen se montra peu efficace en comparaison du curettage dans les tumeurs épiphysaires à cellules géantes. L'examen histologique révéla une transition régulière, graduelle entre la tumeur à cellules géantes et l'ostéite fibreuse localisée mais il fut impossible d'établir des sous-classes où faire rentrer les diverses étapes du développement de ces tumeurs.

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VASO-SEMINAL VESICULOGRAPHY AND ITS CLINICAL APPLICATION[1]

by

Arne Bertelsen and *H. H. Wandall*

»For many surgeons and physicians
the seminal vesicles do not exist.«
Belfield and *Rolnick* 1926.

Since the introduction of the iodized oil, lipiodol, for broncho- and myelography (SICCARD & FORRESTIER, 1922) the application of endography as a method of examining various organs has achieved wide usage and undergone considerable development within various fields.

At an early date this method was applied in the visualization of the female genitals (CARLOS HEUSER, 1924), but apart from American special urology it has only to a slight extent been employed in diagnosing lesions of the male genitals, the vas deferens, the seminal vesicles, and the ejaculatory duct. The above quoted introduction to BELFIELD & ROLNICK's conclusions being true to this day, the authors have inserted it as an epigraph to the present publication.

Although the roentgenological visualization of the male genitals has not been applied to any great extent, it still may be traced rather far back in time. In 1905 BELFIELD introduced vasotomy as a link in the treatment of inflammatory processes in the male genitals, instilling antiseptics into the vas deferens and the seminal vesicles after having exposed the vas by a small incision on the anterior side of the scrotum and opened the lumen with a longitudinal incision. As is well-known the antiseptics ordinarily in use at that time, collargol and other compounds of silver, are radio-opaque, and it therefore was natural to follow their course through the seminiferous tract by roentgen examination. This resulted in a report on »skiagraphy of the seminal ducts» by BELFIELD in 1913. He describes occlusions in the vas deferens and ejaculatory duct as well as abscesses and fistulas in the seminal vesicles.

BELFIELD & ROLNICK (1926) continued the earlier investigations of BELFIELD — still with a special view to the therapeutic effect caused

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by instillations of antiseptics into the seminiferous tract, and in 64 cited cases using »iodol» and »thymol iodide» they found that the materials mentioned quickly cleaned the seminal tract of gonococci and pyogenic bacteria. As to the endographic picture the authors state that the media in question give good, though not so dense roentgenograms. At the same time they warn against using the more radio-opaque materials, lipiodol and iodipin, because of their long persistence in the tissues, which may give rise to cicatrix formation. Iodol and thymol iodide which are iodine solutions in cod liver oil should be less harmful to the structures than lipiodol.

SARGENT (1929) further describes the vaso-seminal vesiculographic findings on the basis of 200 cases using the BELFIELD technique. He finds that 2—3 cc. of thymol iodide are sufficient to fill the vas deferens and vesicles, and that an excessive amount of contrast material forcing the delicate sphincter of the colliculus seminalis and flowing into the urinary bladder may prove the patency of the ejaculatory duct. On the normal film the *vas* runs quite straight until it leaves the lateral wall of the pelvis; at this juncture it as a rule forms several small coils before again running straight and almost taking on the form of a spiral before joining the excretory duct of the seminal vesicles. This place is frequently the site of small diverticula. The *seminal vesicle* consists of fine tubule-like cavities with a central main duct. The *ejaculatory duct* is short and straight, almost threadlike. Like BELFIELD the author finds that the vesicula and ampulla ductus deferentis empty in the course of a few days, generally 2—5 days, caused by continuous peristalsis — an observation which explains the frequent findings of spermatozoa in the urine of normal men. Pathologic conditions like stenosis of the vas may involve a defective filling of the vesicle and the vas centrally to the stenosis. According to SARGENT such stenoses most frequently are encountered at the transition between the lateral and medial part of the intra-pelvic vas deferens. Chronic vesiculitis is revealed by partial or total dilatation of the vesicle and protracted retention of the contrast material — often for weeks. In one case the retention of the contrast material in the cavity revealed an almond-sized perivesicular abscess. The diagnosis was later verified by operation. Finally atrophy or shrinkage in the seminal vesicle have been demonstrated in a number of cases of cured inflammatory processes. Having been able to demonstrate such chronic changes in several cases of chronic polyarthritis SARGENT considers an undiagnosed vesiculitis to be no rare source of focal infection.

The diagnostic possibilities offered by vaso-seminal vesiculography are further proved by the results of 127 examinations published by WILHELM (1939). The contrast medium used was iodochloral which in

no case gave rise to clinical or histological signs of irritation or inflammation. A satisfactory vesiculogram was obtained in 121 cases. The material in question contains diagnoses partly of inflammatory processes in the seminal vesicle (cysts, perivesicular abscesses, tuberculosis), partly of stenoses in the vas deferens or ejaculatory duct. After transurethral prostatic resections it is thus not rare to find an ejaculatory duct obstruction with retention of the contrast medium for months, even for more than a year.

The method of examination used by all the above-mentioned authors has been vasotomy. Contrary to this MERRICKS (1940) employs the transurethral approach catheterizing the ejaculatory duct through which he injects the contrast material. The roentgenograms inserted in the paper are a proof of the good and easily interpretable pictures obtainable by this method. The changes occurring in case of inflammatory processes also are in accordance with the above description by SARGENT with retention of the contrast medium and dilatation of the ducts. In the author's opinion the method also is of therapeutic significance, giving a good drainage of the vesicles as well as a chance of curing a possible ejaculatory duct stenosis — a frequent cause of aspermia.

The publications at hand thus serve to demonstrate that endography is particularly well suited for the examination of the male genitals and that the examination may be effected either as a direct passage examination injecting the contrast material through a vasotomy or by retrograde filling of the tract by catheterization of the ejaculatory duct. According to the material available vaso-seminal vesiculography affords details as to the patency of the seminiferous tract and disease conditions in its various sections — the transurethral method mainly in case the changes are situated in the seminal vesicles or ejaculatory duct.

Authors' Own Investigations

The investigations reported below were started as passage examinations in connexion with operations for male infertility, i. e. vaso-epididymostomy (cf. BERTELSEN & VARNEK 1944) and have therefore in all cases been carried out by injection of the contrast medium through vasotomy. In a number of cases it was possible to insert a fine hypodermic needle percutaneously into the vas deferens, a quite characteristic »sliding» feeling in the fingers announcing that the nozzle of the needle is in place in the lumen. Normally the contrast medium may be injected without difficulty, but in case of an occlusion it meets with considerable resistance and tends to flow backwards along the needle and thereby to spread in the loose tissues of the spermatic cord. This has happened in the case of two patients with subsequent swelling and soreness, but

without suppuration. Furthermore, considering that a quite slight oozing of the contrast medium into the tissues completely obscures the film, we think that the method of choice in all cases should be vasotomy, exposing the vas deferens through a small scrotal incision immediately proximal to the testis. A fine needle is then inserted into the bared vas and 3—5 cc. of the contrast material are injected.

On account of their lengthy persistence in the tissues the iodized oils must beforehand be considered unsuited as *contrast media*, and the choice has therefore been between the two contrast materials, *Hippodin* (trade name for a 50 per cent solution of sodium ortho-iodine hippurate) and *Perabrodil* (trade name for 3-5-diiodide-4-pyridon-N-diethylamine acetate) which both are soluble in water and ordinarily used in this country. The material used must in no way have a harmful effect on the epithelium of the seminiferous tract. The irritative effect of Hippodin, as demonstrated by the following experiment, has therefore been the deciding factor in our choice of Perabrodil as a contrast medium in vaso-seminal vesiculography.

5 cc. of *Hippodin* were injected into two rabbits into the vasa deferentia exposed close to the testes. Segments of the vas were resected on the 2nd, 4th, 10th, and 14th day, the ampulla and the pelvic part being excised at autopsy on the 21st day. The resected samples were divided into several blocks and a series of sections made of each block. The specimens of the samples excised on the 2nd day revealed round cell infiltration, especially eosinophilia, in the wall of the vas, whereas the epithelium was well-preserved everywhere. The specimens from the 4th day, on the other hand, revealed complete desquamation of the epithelium and slight fibrosis of the submucosa, whereas the specimens from the 10th day showed quite slight submucous fibrosis and those from the 14th day no pathological changes.

The effect of *Perabrodil* on the epithelial lining of 4 rabbits has been investigated by the same procedure. Segments of the extrapelvic parts of the vasa were examined on the 2nd, 4th, 7th, 10th, 11th, 14th, and 17th day, the ampullar part being examined during a period extending from the 17th to the 28th day. No pathological changes could be demonstrated in any of the specimens.

Our experiments thus prove that *Hippodin may have a detrimental effect on the epithelium of the vas deferens, an effect which could not be demonstrated when using Perabrodil.* Perabrodil, therefore, should be preferred as a contrast medium in the roentgen examination of the male genitals, permanent changes in the epithelium of the seminiferous tract caused by the use of Hippodin not being out of the question.

Material and Results

Vaso-seminal vesiculography was carried out in a total of 16 cases. In 6 cases the examination was made on patients during vasectomy, in the remaining 10 cases the examination was effected for diagnostic purposes, the patients in question suffering from diseases referable to the genital system.

Fig. 1. Fig. 2.

Fig. 1. Normal vaso-seminal vesiculogram with delicate, straight vasa deferentia and tortuous vesicles.
(Dept. C, patient No. 1447/43, aged 27, vasectomized on account of imbecility.)

Fig. 2. Normal vaso-seminal vesiculogram. Vesicles more plain, the vas forming rather large coils.
(Dept. C, patient No. 1823/43, aged 18, vasectomized on account of imbecility.)

The following description of the normal vaso-seminal vesiculographic findings (see Figs. 1 and 2) is based on the results of the examination of the 6 above-mentioned patients, who were admitted to the Department and submitted to bilateral vasectomy on account of imbecility.

Speaking about the *vas deferens* a distinction must be made between its extra- and intra-abdominal course the annulus ingvinalis subcutaneus forming the borderline. By fastening a hypodermic needle into the tuberculum pubicum during the sittings the projection of the annulus ingvinalis subcutaneus was found to be 1 cm. below the upper edge of the foramen obturatum, approximately at the medial border of the latter. From this point the vas runs along the linea terminalis, bending about the middle of the latter towards the centre of the pelvis, frequently forming several major or minor coils. Along the entire course mentioned it is quite thin and of the same caliber. On a level with the ampulla the dimension grows larger and at the same time it coils up forming the ampullar spiral uniting with the excretory duct of the seminal vesicle.

The *seminal vesicle* often presents a very irregular picture on account of the tortuous canals. As a rule the caliber is rather uniform, but dilatations almost to the extent of diverticula may also appear in the otherwise uniform-sized canals (Fig. 4). Although rarely, vesicles of a quite simple construction do occur, in which case there may be constrictions

Fig. 3.

Fig. 4.

Fig. 3. Normal vaso-seminal vesiculogram with large, coarse vesicles, kinked vasa and separate ejaculatory duct for each side.
(Dept. C., patient No. 804/44, aged 22, vasectomized on account of imbecility.)

Fig. 4. Vaso-seminal vesiculogram with coarse vesicle and tortuous intrapelvic vas.
(Dept. C, patient No. 1150/44, aged 20. Diagnosis: Undescended left testis.)

dividing the vesicle into major and minor sections (Fig. 3). Considering this great variation some caution should be exercised in diagnosing changes of a slight extent in case of presumed disease conditions in the vesicle. SARGENT perhaps attaches too much importance to dilatation as a basis for a diagnosis of chronic vesiculitis (cf. Fig. 3 of a 22-year old vasectomized patient).

The junction of the *excretory duct and the vas deferens* has in all cases been distinct. In 4 cases the canals from both sides united in a typical *ejaculatory duct* (Fig. 1) which could be traced until it opened into the urethra. In 2 cases there was an ejaculatory duct for the canals of each side, opening into the urethra side by side (Figs. 2 and 3). In all cases a flow of contrast material into the urethra and bladder has been evidence of the patency of the tract.

As apparent from the above the normal vaso-seminal vesiculogram is quite characteristic, and pathological conditions in the form of obstructions are distinctly visible, whereas inflammatory processes in the vesicle are more difficult to discern. On account of the marked variation in the shape and caliber of normal vesicles the processes mentioned are not so easily diagnosed in case they cause but minor deviations in shape.

Fig. 5.

Fig. 6.

Fig. 5. Vaso-seminal vesiculogram with a block (indicated by the arrow) in the filling of the vas in the position of the annulus ingvinalis subcutaneus.
(Dept. C, patient No. 1038/43, aged 38. Diagnosis: Aspermia following herniotomy.)

Fig. 6. Hypoplastic seminal vesicle.
(Dept. C, patient No. 636/44, aged 30. Diagnosis: Aspermia (trauma 10 years previous to admission to hospital.)

Vaso-seminal vesiculography has been performed as a diagnostic measure in the case of 10 patients grouped as follows:

Sequel of herniotomy (1 suffering from aspermia, 1 from oligospermia, 2 from pain in the groin and testis on the operated side)	4
Aspermia following trauma to testis and epididymis	1
Sequel of epididymal resection	1
Undescended testis	2
Vesiculitis	2
Total	10

Obstructed passage through the vas deferens was demonstrated in 3 patients, all operated on for inguinal hernia by the Bassini method. In all 3 cases there was a characteristic conical filling defect at the position of the entrance of the spermatic cord into the inguinal canal (Fig. 5) and flow of contrast material into the distal end of the vas and epididymal duct.

Abnormal course, but patency of the vas deferens was demonstrated in 2 patients with undescended testis. In these cases the vas, which everywhere was of a uniform caliber, was quite extraordinarily tortuous on the route from the inguinal canal to the ampulla (Fig. 4).

Changes in the vesicles like those described by SARGENT, BELFIELD, BELFIELD & ROLNICK, WILHELM, and MERRICKS could not be demonstrated. Neither dilatation of the canals nor retention of contrast medium was observed in the two cases of clinically proved seminal vesiculitis (exploration revealed tender vesicles as thick as thumbs).[1]

Insufficient development of the seminal vesicles was found in 3 cases (1 with undescended testis, 1 with aspermia following trauma to testis and epididymis, and 1 with resected epididymis on account of epididymitis). We are not prepared to say whether such a finding is of any clinical importance, but it seems reasonable to presume that it is a result of the inactivity due to the arrested or reduced function of the seminal duct in question.

On the basis of the above, vaso-seminal vesiculography for diagnostic purposes must be considered to be called for in the following cases:

(1) *Patients with aspermia*, but preserved testicular function. It is true that there are opponents against the application of vaso-seminal vesiculography in connexion with vaso-epididymostomy in cases of aspermia (cf. HAGNER) contending that this form of examination may compromise the operative result by damaging the seminal epithelium. Our experiments, however, having proved that this is hardly the case when using Perabrodil and SARGENT having been able to demonstrate normal sperms in all his 16 cases in spite of vaso-seminal vesiculography, the latter should no doubt in future be included in the examination of patients suffering from aspermia. This fact is further supported by the assumption advanced by MERRICKS that an obstruction of the ejaculatory duct is the most common cause of aspermia.

(2) *Patients with seminal vesiculitis.* In a number of cases vaso-seminal vesiculography will be able to afford information as to the presence of morbid processes in the vesicle by revealing the shape and maybe defective evacuation of the latter. This could attain special importance in cases where there could be a question of tuberculous foci as the source of a tubercle baciluria. The question concerning the risk of spreading tubercle bacilli by this method is being further investigated.

(3) *Adults about to be submitted to orchidopexy* it being important to find out whether the vas deferens is sufficiently long in order that the desired segment may be mobilized. In the case of children the examination is neither called for nor warrantable.

[1] Pathological conditions in the seminal vesicle or the excretory ducts have been observed since this paper was written. Roentgen examination revealed in one case of haemospermia a fistula originating in the right ejaculatory duct, and in one case of vesiculitis no filling of the left seminal vesicle.

(4) *Patients with pain in the groin and testis following herniotomies* the vesiculogram revealing whether a possible constriction in the vas may be the cause.

Vaso-seminal vesiculography is a small intervention which may afford information of decisive influence on the treatment. It is therefore reasonable to wish that this form of endography in future should form part of the examinaton of the male genitals.

SUMMARY

The Roentgen examination of the male genitals may be performed by injecting contrast medium either into the vas deferens through vasotomy or by the transurethral approach into the ejaculatory duct. Information is obtained partly about the patency of the system, partly about the existence of disease conditions of other kinds. The authors have employed the first method in the case of 16 patients: 6 were submitted to the examination during vasectomies for the purpose of gaining a basis for the interpretation of the normal vaso-seminal vesiculogram, and 10 on account of various affections in the genital system. This method of examination was found to be applicable especially in case of (1) patients suffering from aspermia, (2) patients suffering from seminal vesiculitis, (3) adults about to be submitted to orchidopexy, and (4) patients suffering from pain in the groin or testis following herniotomy. The authors propose that vaso-seminal vesiculography in future may form part of the examination of the male genitals.

ZUSAMMENFASSUNG

Die Röntgenuntersuchung der männlichen Geschlechtsorgane kann durch Einspritzung von Kontrastmittel entweder nach Vasotomie in das Vas deferens oder auf dem transurethralen Wege in den Ductus ejaculatorius stattfinden. Man erhält Auskünfte teils über die Durchgängigkeit des Systems, teils über das Vorliegen von Krankheitszuständen anderer Art. Verff. haben die erstere Methode an 16 Patienten verwendet: bei 6 wurde die Untersuchung gelegentlich einer Vasektomie vorgenommen, um eine Basis für die Auffassung von dem normalen Röntgenbild des Samenleiters und der Samenblase zu schaffen, und bei 10 wegen verschiedener Krankheiten der Genitalorgane. Diese Untersuchungsmethode hat sich besonders bewährt (1) bei Kranken, die an Aspermie leiden, (2) bei Patienten mit Samenblasenentzündung, bei (3) Erwachsenen, an denen eine Orchidopexie vorgenommen werden soll, sowie (4) bei Kranken, die nach einer Herniotomie an Schmerzen in der Leistenbeuge oder im Hoden klagen. Verff. schlagen vor, dass die Röntgendarstellung des Samenleiters und der Samenblase in Zukunft ein Bestandteil der Untersuchung der männlichen Geschlechtsorgane werden soll.

RÉSUMÉ

On peut pratiquer l'examen radiologique des organes génitaux masculins par l'injection d'une substance opaque soit, après vasectomie, dans le canal déférent, soit par voie transurétrale dans le canal spermatique. On se renseigne ainsi et sur la présence d'obstacles dans le système, et sur l'existence d'états pathologiques d'autre nature. Les auteurs ont utilisé la première méthode dans 16 cas; dans 6 cas, ils pratiquèrent l'examen après vasectomie afin d'établir une base pour l'interprétation de l'image radiologique

normale du conduit spermatique et de la vésicule séminale et dans 10 autres cas pour diverses affections des organes génitaux. Cette méthode d'examen a démontré sa valeur chez (1) les malades atteints d'aspermie, (2) dans les cas d'inflammation de la vésicule séminale, chez (3) les adultes devant subir une orchidopexie ainsi que chez (4) les malades présentant des douleurs de la région inguinale après herniotomie. Les auteurs proposent que l'image radiologique du canal spermatique et de la vésicule séminale fasse à l'avenir partie de l'examen des organes génitaux masculins.

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FROM THE CHILDREN'S HOSPITAL, FUGLEBAKKEN, COPENHAGEN
(CHIEF: VALDEMAR POULSEN, M. D.)

SOME PRACTICAL HINTS ON THE PERFORMANCE OF UROGRAPHY ON INFANTS[1]

by

Harald Christiansen, M. D.

Urography is used to some extent also in the case of infants, and is necessary especially in chronic affections of the urinary tract. To the roentgenologist, these examinations present several technical problems, which studies of the literature do not help him to solve. One must build on own experiences or seek guidance from colleagues working in some hospital department for children's diseases. In such services there is gradually developed a technic which may be of assistance to others, who more seldom are called upon to make these examinations.

Any more or less elaborate preparation, as in the case of adults, is impracticable in the case of small children; but copious defecation and fasting for 3—4 hours before the examination will also be sufficient. The administration of chloral as a quieter is often a disappointment; and is, in fact, unnecessary with the efficient apparatus now used.

The contrast substance is best applied intravenously. The cubital veins of the plump arms are, as a rule, not accessible, and unless they are visible the idea of injecting there may as well be abandoned first as last. Also injection through the fontanel, into the superior sagittal sinus, must be advised against; for if the hypertonic contrast medium is by mistake injected into the subdural space the result may be mortal. The best veins into which to make the injection are the superior temporal and its branches. The child is placed on a pillow, with the head hanging outside its edge; there will then come some stasis in these vessels, which will be further increased when the child now begins to cry. A rather fine cannula, like a morphine cannula, may be used; but it must be fitted with a thin india rubber tube, 10—15 cm. long, into the free end of which the record syringe with the contrast fluid is inserted; there will then be no risk of the cannula becoming displaced by manipulations with the syringe, after it has been introduced in the vein.

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Fig. 1.

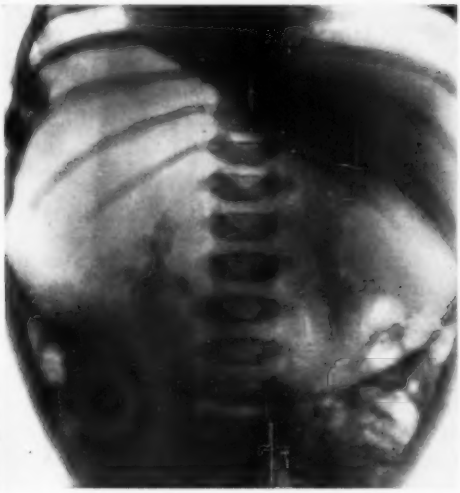

Fig. 2.

Fig. 1. The contrast medium during the injection into the marrow cavity of the tibia.
Fig. 2. The distended stomach, through which the pyelograms are seen.

Sometimes one may meet with a case in which it is impossible to do the injection intravenously, and one may then be tempted to inject in the muscle. But according to our experience this is to be deprecated, because it too often results in abscesses or necroses, no matter whether the contrast medium is diluted or not. These necroses heal slowly and make the relations mistrustful, and we therefore no longer use intramuscular injection. Instead, the contrast medium may in these cases be made *intraosseously*. Intrasternal infusion of blood and saline solution has long been common, and the idea of injecting also the contrast fluid in this manner readily suggests itself. On infants, the injection cannot be made into the marrow cavity of the sternum, however, because it is so little developed; but it can be made into that of the tibia; the usual sternal cannula being introduced into the medial facies, just below the medial condyle, and the fluid being injected slowly, with a record syringe. Already during the injection, the contrast medium is seen in the deferent vessels, and the excretion through the kidneys takes place just as readily as in the case of intravenous injection. It is, however, a method of application which one will no doubt use only exceptionally, on account of the risk of infection.

Though the injection on infants may be troublesome, this is nothing compared with the overwhelming difficulty which the gas-filled loops

of intestine present when it comes to interpreting the pyelograms. The air which the child has swallowed during its crying, together with the contents of the gut, fills both the small and the large intestine; and the delicate pyelograms disappear between the folds and contours of the passage, or blend with them, so that one often is unable to say whether there is anything abnormal, unless there is a serious hydronephrosis. In such cases we make use of the enormous capacity for expansion possessed by the infantile stomach. Just before the exposure we give the child from 30 to 50 milliliters of apollinaris sweetened with saccharin. It is given with a teaspoon, and there is no difficulty in getting the child to swallow it. The result is astonishing. The stomach gets so distended that it presses the intestines down into the distal half of the abdomen, and through the air of the stomach the pyelograms stand out without disturbing overlayings. If the distension of the stomach is not great enough, the child may be given more soda-water, We have never observed any ill effects from this procedure. On the contrary, this little improvement in the technic of urography has been of great assistance and is far superior to the help one has of compression, which is difficult to practice on children and only makes them still more nervous and restless.

As we have in a couple of cases observed some periosteal reaction when the undiluted uroselectan B was injected into the bone marrow, it may be noted that LENNART WALLDÉN in the Acta Radiologica vol. XXV, fasc. 3, June 30th, 1944, states that by dilution of uroselectan B with sterilised water at the ratio 8 : 1—10 : 1 an approximately isotonic solution is obtained, which can be injected into the bone marrow without causing noticeable discomfort to the receiver.

SUMMARY

In urography of small children, the author recommends that the patient before the exposure is made be given apollinaris to drink. This causes the stomach to distend, so that the pyelograms are seen through the gas in the stomach, without interference from overlying intestines.

ZUSAMMENFASSUNG

Bei Urographie bei kleinen Kindern schlägt Verf. vor, dem Patienten vor der Aufnahme Apollinaris zu trinken zu geben. Dies führt zu einer Aufblähung des Magens, wobei das Pyelogramm durch das Gas im Magen hindurch sichtbar wird, ohne Störungen seitens überlagernder Darmschlingen.

RÉSUMÉ

L'auteur recommande de faire boire de l'eau gazeuse aux enfants en bas âge juste avant la prise du cliché d'urographie. Ainsi l'estomac se distend et la pyélographie se projette sur le gaz stomacal, sans interposition d'intestins susjacents.

FROM THE RADIOLOGIC SERVICE OF THE CENTRAL HOSPITAL FOR FREDERIKSBORG COUNTY, HILLERØD, DENMARK (CHIEF: SV. A. CHROM, M. D.)

ON THE INCIDENCE OF OSTEOCHONDROSIS[1]

by

Sv. A. Chrom

The increasing interest taken in recent years in the lumbago-ischias syndrome, and in the nucleus prolapse as etiologic factor for ischias, has noticeably increased the number of roentgen examinations of the vertebral column, particularly of the lumbar region.

Among a material of patients sent to be roentgen-examined on account of lumbar pains, or lumbar pains combined with pains of an ischiatic character, one not infrequently finds a roentgenologic picture characterised by narrowing of some intervertebral disk, oftenest the 5th lumbar, accompanied by osseous changes in the form of sclerosis of the borders of the vertebral bodies involved and typical exostosis formation on the anterior border of one or both of these bodies (see Fig. 1). In some cases the picture is, moreover, complicated by a displacement of the two bodies in relation to each other, which in lateral views makes it look like the picture of a spondylolisthesis. These changes are typical for the affection called osteochondrosis, which has been thoroughly investigated and described by SCHMORL & JUNGHANS. To recognise their presence is in itself not difficult; the difficulty arises when it becomes a question of evaluating the finding in relation to the clinical picture. The present paper is an attempt to throw light on some of the problems involved, by means of a year's patient-material.

Of Scandinavian authors, F. KNUTSSON and VOGT have given thorough descriptions of osteochondrosis, while affections of the disks have been the object of studies by two Danish writers, K. OVERGAARD and O. WISSING.

According to SCHMORL, the affection begins with a diminution of the fluid content of the pulpy nucleus, resulting in the formation, in the latter, of cracks and fissures running in all directions, which sometimes can be recognised in the roentgenograms owing to their content

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of air (vacuum phenomenon); whereby it, as pointed out by KNUTSSON, becomes possible to diagnose an incipient osteochondrosis. If the process progresses, the nucleus shrinks and gradually loses its elasticity and ability to expand; and at the same time the height of the disk diminishes. The degenerative processes are, however, confined to its central part whereas the fibrous ring remains intact. But as result of the collapse of the disk and the reduced or entirely lost capacity of the nucleus for expansion, the fibers of the ring become slack, and thus a possibility arises for the vertebral bodies to become slightly dislocated in relation to each other. To the continuous small traumata to which their surfaces thereby become exposed, they react by sclerosis. The slackening of the fibers of the ring readily explains the possibility for displacement of the vertebral bodies in relation to each other, as result of which a so-called pseudospondylolisthesis may develop.

From this description it will be understood that it only in few, rare cases will be possible to make the roentgenologic diagnosis of degeneration of the disk on the basis of the cartilaginous changes alone, and that the diagnosis can only be established after the secondary, reactive processes have developed.

As the affection may be found in very different stages of development, it cannot, of course, be expected that all the secondary changes mentioned will be represented in all the cases; but it must be emphasised that a diminished disk as only finding is of no value whatever in this connexion. This applies especially where the question is of the 5th lumbar disk; because this, owing to variations in the shape and position of the 5th lumbar vertebra, physiologically is liable to vary a great deal in height.

In young individuals one may find the picture of osteochondrosis described above, without immixture of disturbing elements; but oftenest there will, besides, be changes in the vertebral column, due to a spondylosis deformans. As an aid to distinguish between the two pathologic pictures it must be remembered that the last-named disease is conditioned on degeneration in the peripheral part of the disk, that is of the fibers of the ring. These fibers break, and the disk then bulges outwards, because the elasticity of the pulpous nucleus usually is preserved. The result is a pressure on the anterior longitudial ligament, which is transmitted to the attachments of the latter on the bodies of the vertebrae, a little centrally to their borders. Here, the bone reacts by new bone formation, and the well-known beak-shaped exostoses develop. The appearance of these, and the place in which they arise, thus distinguish them from the exostoses that develop in the case of an uncomplicated osteochondrosis, where it is a question of a lip-like prolongation of the margin of the vertebral body itself. In the great majority of cases one will find mixed forms; but if the anatomical features and the underlying

pathoanatomical conditions are borne in mind there will nevertheless be great possibility of being able to distinguish between the different elements of the two pathological pictures.

Also inflammations, both acute and chronic, as well as malignant tumors, may cause degeneration of the disks; but in such cases pronounced halisteresis, ostitis or periosteal new formations, together with the history of the case, will soon put one on the right track.

In the first year since the radiologic service of the Central Hospital for Fredriksborg County came into operation, 132 patients have been referred to us for roentgen examination of the vertebral column, on the most different indications. Of these patients, 50 were women, 82 men. Their distribution according to age groups was as follows:

Fig. 1.

	20—29	30—39	40—49	50—59	60—69	70—79	80—89
Women	8	8	13	11	8	2	
Men	6	25	22	18	5	5	1

In 20 of these 132, a quite characteristic picture of osteochondrosis was found. For comparison it may be noted that TAMMIA among 388 patients with symptoms referable to the vertebral column found 25 cases. In 17 of these, the 5th lumbar disk was the seat of the osteochondrosis; in our material, 18 out of 20 cases had this location. Eleven of these 20 patients were men, 9 women. Their distribution according to age was:

	30—39	40—49	50—59	60—69	70—79	80—89
Women	2	3	3	1		
Men	2	3	3		2	1

Fifteen of the 20 had been admitted to medical services with such diagnoses as lumbago, recurrent lumbago, ischias and to observation for nucleus prolapse. Four of them had, however, primarily been admitted

in order to be treated respectively for struma, bronchopneumonia, kyphoscoliosis (obs. for cardiac affection), and abdominal tumor; but they had all four stated to the journal that they had been troubled with lumbar pains for several years, and roentgen examination of the vertebral column was therefore clearly indicated. The remaining 5 patients of this group had been referred as ambulant cases with the diagnosis of lumbago.

It might now be interesting to see if similar changes in the vertebral column would be found in patients who did not complain of symptoms referable to that region; in other words, whether roentgenologic changes like those typical for osteochondrosis could be found as an incidental feature. If this should be the case, it would not be without interest to get an impression of the frequency of such a finding.

When one has occasion to study many films of the vertebral column, one often finds marked, or even enormous, spondylosis deformans, and is surprised to see how few symptoms (if any) these changes elicit. This always results in great uncertainty when it becomes a question of comparing a finding in spondylosis deformans with anamnestic information about pains referable to the vertebral column. If the same should be the case with regard to osteochondrosis, there would here be the same uncertainty about the evaluation of the roentgenologic findings.

Fortunately, every radiologic service has on hand a serviceable control material, inasmuch as most of the lateral views from the examinations of the colon give an excellent picture of the 5th lumbar disk; and since the osteochondrosis is in the great majority of cases located there, the material is well suited to the purpose.

In the past year, examinations of the colon with injection of contrast fluid have been made on 79 patients above the age of 30 years. Sixteen of these examinations are not considered in the present connexion, because the 5th lumbar disk is not seen distinctly in the lateral views. Of the remaining 63 patients, 37 were women, 26 men. Their distribution according to age corresponds with that of the patients on whom examination was made of the vertebral column.

	30—39	40—49	50—59	60—69	70—79	80—89
Women	11	9	10	6	1	
Men	7	5	6	3	4	1

It was now found that, of these sixty-three patients, there were two whose roentgenograms showed changes typical of osteochondrosis.

One of them was a female domestic-service teacher, aged 64 years, who was admitted to the medical ward on Dec. 2nd, 1943, for diabetes mellitus and arterial hypertension. In 1921, glycosuria had been ascertained, and in 1932 she had begun to get insulin treatment. In the same year she fell over a bucket, hurting her left flank, and after that got radiating pains in the left lower extremity. In 1932, 1935 and 1942 she was in hospi-

tal to be treated for ischias, and was given physicotherapeutic treatment of various kinds. At admission Dec. 2nd, 1943, she did not complain of pains in the loin or radiating into the lower extremities. As she also suffered from chronic obstipation, an examination of the colon was made, with injection of contrast enema, and on that occasion osteochondrosis of the 5th lumbar disk was diagnosed, as an incidental finding. When she later was admitted again, on March 8th, same year, she complained of grumbling pains over the left flank and radiating down on the posterior side of the left femur.

The other patient was a coachman, 47 years old, admitted March 28th, 1944, with the diagnosis of abdominal disorder, obs. for pulmonary tuberculosis. He stated that he had been well until 3—4 months before admission, when he had begun to suffer from fatigue, loss of appetite and weight, and pressure across the abdomen without any relation to the meals. As the case was obscure, various examinations were made, among others of the colon with contrast enema; and by this typical changes of the 5th lumbar disk were found, with narrowing of the latter, marginal sclerosis and lip-like prolongation of the border of the 5th lumbar vertebra. Laparotomy was done, and the case diagnosed as chronic, infectious hepatitis. The patient had not at any time had lumbago or pains of ischiatic character, and did not remember ever having sustained any violent trauma to the vertebral column.

Of these two cases, the first belongs to the first group and only by chance happens to figure among the controls. There thus among the 63 remains only 1 in which the osteochondrosis occurred as an incidental finding. In the first group, of patients with complaints referable to the vertebral column, there are 20 cases of osteochondrosis among 132 examined; that is a ten times greater frequency. This seems to indicate that osteochondrosis is not a finding of doubtful clinical significance, but an affection which should be the object of thorough examination and treatment.

The roentgenologic changes in this disease are easy to recognise. In the 22 cases (including the two from the control group) the different characteristics were present as follows: Narrowing of the disk and marginal sclerosis in all 22, lip-like marginal exostosis in 19, displacement of the bodies of the vertebrae in relation to each other in 6. After what has been exposed in the foregoing it is not surprising that there should be narrowing of the disk and marginal sclerosis in all the cases. In 3 cases there was no lip-like marginal exostosis; in one of these there was prolapse of the nucleus posteriorly, as seen by air-myelography and afterwards verified by operation. In this case there was thus both central and peripheral degeneration of the disk; what may be imagined to have been the reason why there was no development of marginal exostosis; but the material is to small to justify any conclusions in that respect. The two other cases were complicated by spondylosis deformans. Displacement was demonstrated in 6 cases. In four of them the body of the upper vertebra had slid forwards, in the two others it had become displaced backwards. In all the six cases the other three characteristics named above were present.

In the modern diagnosis of conditions in the vertebral column one is often confronted with the question whether there is prolapse of the nucleus. The examination which settles this is air-myelography; but it would be of value to know whether the ascertainment of osteochondrosis makes the existence of nucleus prolapse more likely in the given case. Air-myelography was done in 7 of the 20 cases where there was osteochondrosis; in them all the finding was positive, and in 6 of them the finding was verified on operation. An analysis of the roentgenograms of the seven cases shows nothing which distinguishes them from the roentgenograms of the 13 others, in which there was no indication for air-myelography.

If we review the twenty case histories with regard to the stated onset of the pains, their localisation and possible radiation, the picture is variegated and confusing and contains nothing which might serve as basis for conclusions respecting possible complications of osteochondrosis with prolapse of the nucleus. Only by air-myelography, as supplement to the roentgenologic examination, will it thus be possible to get any information of whether such a complication exists.

In the case of a couple of elderly patients, roentgen treatment was given with good palliative effect; 150 r × 4; filter, 0.5 mm. Cu. + 3 mm. Al.; distance, 40 cm.; 170 kv. to a field of 8 × 10 cm, straight in.

SUMMARY

The author describes the roentgen picture and the pathoanatomical changes in osteochondrosis. Among 132 patients with complaints referable to the vertebral column, 20 cases of this disease were found, while a control material from examinations of the colon showed 1 case among 63 examined. The roentgen picture gives no information respecting possible complication with prolapse of the nucleus; such information can only be obtained by means of supplementary air-myelography.

ZUSAMMENFASSUNG

Verf. beschreibt das Röntgenbild und die pathologisch-anatomischen Veränderungen bei Osteochondrose. Unter 132 Kranken, deren Klagen auf die Wirbelsäule zurückgeführt werden konnten, wurden 20 Fälle dieser Krankheit gefunden, während in einem Kontrollmaterial von Wirbelsäulenuntersuchungen unter 63 Untersuchten nur 1 Fall vorkam. Das Röntgenbild gibt keine Auskünfte inbezug auf einen eventuellen Zwischenwirbelscheibenprolaps als Komplikation. Hierüber kann nur die zusätzliche Luftmyelographie Aufschlüsse geben.

RÉSUMÉ

L'auteur décrit l'image radiologique et les lésions anatomo-pathologiques de l'osteochondrose. Parmi 132 malades dont les plaintes pouvaient faire admettre des désordres du côté de la colonne vertébrale, on trouva 20 cas de cette affection, alors qu'un matériel

de contrôle constitué par 63 colonnes examinées n'en comprenait qu'un seul. L'image radiologique ne renseigne nullement sur la possibilité d'un prolapsus discal venant compliquer l'affection; seule l'adjonction d'une myélographie par injection d'air peut donner des éclaircissements sur ce point.

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INVAGINATION OF THE STOMACH[1]

A Case Diagnosed by Means of Roentgen Examination

by

Kai Dohn and *Börge Faber.*

In the Danish literature only one case of invagination of the stomach has been previously reported (FABRICIUS-MÖLLER, 1918) and it was only diagnosed on post-mortem examination. In the present case the diagnosis was established in vivo on the basis of a characteristic roentgenogram.

The writers' case:

A. M. N. born on Sept. 6th, 1872. Medical ward 811/44.

On June 7th, 1944, a woman, aged 71, was admitted to the medical ward for anaemia gravis. The pt. had been previously in good health, she had had one normal partus 48 years ago. 5 months before admission the patient had slight, pungent pain for a couple of weeks coming on periodically across the upper part of the abdomen, radiating towards the back. The pain was not associated with the meals, she could eat any food without inconvenience, and there was no nausea or vomiting. She lost 5 pounds which, however, she soon put on again.

The pt. then felt quite well until the last fortnight before admission, when similar pain again occurred. The pt. had become increasingly pale, felt very tired and giddy and had fainted a couple of times. The temperature had been slightly increased. The motions had always been somewhat sluggish but are said never to have been melenic. On admission the pain had subsided and the pt. only complained of fatigue.

The objective positive findings were as follows: Tp. 38°. Pulse 110. State of nutrition rather over the average. The pt. was tired and exhausted, highly anæmic with a waxy pale complexion. In the abdomen an indefinite resistance was palpated over the umbilicus. On rectal exploration no tumours were felt, but there were dark fæces (+ Bz) on the finger.

The preliminary diagnosis was a hemorrhagic anæmia as a consequence of cancer of the alimentary canal.

The following are some of the results of the examination on admission:

Sedimentation test: 45 mm./1 h. Hb. 28 per cent. Red blood corpuscles: 1.60 mill. Colour index: 0.88. Halometry: 7.5 μ. Leucocytes: 7 900. Differential count: Normal distribution. Sternal puncture showed signs of severe simple anæmia (hemorrhagic anæmia)

[1] Submitted for publication, Sept. 26, 1944.

(sign. SÖEBORG OHLSEN). No pathologic constituents in the urine. Roentgen examination of the colon showed normal conditions. *Ewald's test meal:* $^{8}/_{6}$ and $^{9}/_{6}$ ($^{3}/_{4}$ of an hour): 47 + 25 ccm, slightly chymified with ample mucus. K/Ph: 0/13. Feces: + Bz., ÷ mucus.

The hemoglobin percentage fell to 17, for which reason blood transfusion was instituted on June 15th, and only then the pt. could be sent down for roentgen examination of the stomach.

Roentgen examination of the stomach: June 16th, 1944. (Fig. 1.)

A picture appears that is difficult to make out. It looks as if the centre part of the stomach is invaginated into the pyloric part and further 6 to 8 cm into the duodenum, so that a real invagination should have occurred. The free part of the stomach is shortened to about 10 or 12 cm. This part of the stomach is only slightly distended and the contrast medium passes quickly on through the invaginated part and runs back around the latter forming a collar-shaped figure in the reduplication. There is no retention in the stomach, as it is almost evacuated in the course of the examination. — 4 h. p. c. the stomach is empty. *R. D.* Invaginatio ventriculi (sign. FABER).

As the general health was bad, as referred to, and as — apart from the occult bleeding — the invagination of the stomach did not give rise to symptoms, especially symptoms of pyloric occlusion, it was decided to wait for the time being and try to improve the pt.'s general health. This was achieved beyond expectation. After energetic antianæmic treatment the hemoglobin rose to 68 per cent. in the course of a month, the temperature fell to normal and the sedimentation test to 9 mm/1 h. 3 weeks after admission the motions were without any blood.

On June 27th the roentgen examination of the stomach was repeated with the following surprising result: (Fig. 2.) Pictures are obtained which display a material difference from those of the first examination. The dominant feature of the picture is now constituted by defects, the size of a small apple, in the shadow of the fundus, presumably caused by one or more stalky tumours. The remaining part of the stomach is to-day seen to be quite natural with a slender pyloric part and a bulbus duodeni of normal shape. The only way in which the two examinations can be made to harmonize seems to be to suppose that a stalky tumour in the fundus part has given rise to the previous invagination, which has now been obviated spontaneously. *R. D.* Tumour ventriculi. (sign. FABER.)

As it was considered probable that the tumour was benign and might cause serious complications again it was intended to have the patient operated on when her general health had further improved. Unfortunately this was prevented by fatal complications of quite another nature. The pt. developed pyuria, which was treated with sulphathiazol, which brought about anuria; the latter was, however, obviated by means of intravenous infusions of saline and fluid, but the pt. died a few days after, on Aug. 6th, from an intercurrent bronchopneumonia.

Post-mortem examination: After opening of the abdomen it appears to be normal, especially the stomach and duodenum are normal without signs of strangulation. Through the stomach wall a stalky tumour, the size of a walnut, is felt in the fundus with the stalk coming from the neighbourhood of the beginning of the greater curvature. With a finger the tumour is easily passed through the stomach, on through the pyloric ring and down to the middle of the pars descendens duodeni, causing invagination of the corpus ventriculi. (Fig. 3.) When the stomach is cut open the said tumour is seen to be the size of a green walnut with a smooth surface and with a stalk, $1 \times {}^{1}/_{2}$ cm. broad and about 1 cm. long. Otherwise the mucous membrane of the stomach is normal. The pyloric ring is wide, easily admitting four fingers. The upper part of the duodenum, too, is wide but otherwise normal.

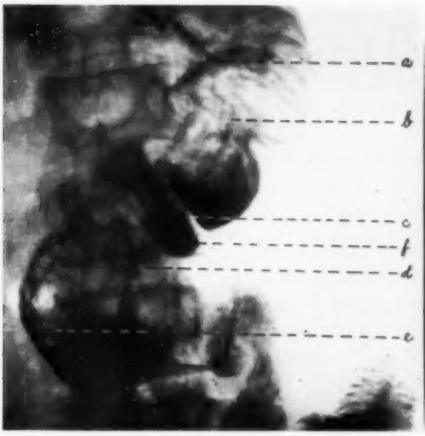


Fig. 1.

Fig. 2.

Fig. 1. Invaginatio ventriculi.
The invagination begins at »a». At »b» longitudinal folds are seen in the intussusceptum, »c» is the pyloric ring. At »d» longitudinal folds are seen in the intussusceptum and transverse folds in the intussuscipiens, »e» is the apex of the invaginated part. At »f» contrast medium is seen in the reduplication between the middle and outer layers of the intussuscipiens.

Fig. 2. The same stomach as in Fig. 1 after spontaneous desinvagination.
At »a» clearing is seen, produced by a stalky tumour (myoma). The remaining parts of the stomach and the duodenum are now normal.

Fig. 3. Post-mortem preparation.
The invagination of the tumour and the stomach is imitated manually, and the invaginated part is seen projecting into the duodenum, corresponding entirely to Fig. 1. »a» is the invaginated stomach, »b» is the duodenum with the invaginated part.

The rest of the post-mortem examination showed nothing of interest in this connection.

Microscopy: The tumour is a leiomyoma with some stasis and interstitial hemorrhage.

On Invaginations of the Stomach

The stomach is invaginated far more rarely than the intestines. The reason is partly that it is relatively well fixed along either curvature, partly that its lumen decreases in width in the direction of the peristaltic movement, and that it is far wider than the adjoining parts of intestine. Lastly, its peristalsis is different from that of the intestines, as the wandering rings of contraction, to which so great an importance to the occurrence of the intestinal invagination is ascribed, are said not to occur in the stomach (LÖNNERBLAD). Correspondingly the invagination of the stomach always occurs as a secondary phenomenon, determined by some primary abnormality, in contradistinction to the intestinal invaginations, which most frequently are of primary, so to speak physiological, occurrence.

The occurrence of an invagination of the stomach is favoured by a flaccid and less well-fixed stomach, great width of the pyloric ring and greater tendency to displacement of the latter and the duodenum (LÖNNERBLAD). Therefore the disorder is most frequently seen in elderly women. Slighter cases of invagination often precede the case leading to the diagnosis being established. This also applies to our case.

Invaginations of the stomach may be *ascending or descending.*

Ascending gastroesophageal invagination has been described by EDERLEN (quoted by FABRICIUS-MÖLLER).

Ascending gastro-gastric invagination has been mentioned by ZDANSKY and is said to be due to a fixation of the pyloric part.

The following types of *descending invagination* of the stomach have been described:

The simplest type is prolapse of the mucous membrane through the pyloric ring (see HENSCHEN's and JENSSEN's publications) and corresponds entirely to the disorder described by KEMP, BOAS and FABER as stenosing gastritis.

The invaginations proper may be *lateral or central*, only part of or the whole of the circumference of the stomach wall being involved in the invagination.

Invagination of the pylorus into the duodenum, which has been described in pyloric spasm (AGATI) and in tumour of the pyloric ring (THOMSEN, LOTSCH, quoted by LÖNNERBLAD) are instances of invaginations which are central already from the onset. The same applies to the

descending ventriculo-ventricular invagination, which has been seen only during agony (ENGEL, quoted by LÖNNERBLAD).

In gastroenteroanastomoses both descending (HENSCHEN) and ascending invaginations may be seen (ADAMS, BONOMINI, CAMERON and MACFARLANE, HENSCHEN, MEISSNER, ZDANSKY). The present publication will not deal with these forms.

The most frequent form of invagination of the stomach, the only form we shall deal with in the following and which our case is an instance of, is represented by *the, right from the onset, lateral descending invaginations in non-operated stomachs*. Simple prolapse of a stalky tumour through the pyloric ring may be considered a precursory stage hereof, and according to EUSTERMAN and BALFOUR (reported by MYHRE) this is said to take place with 10 per cent. of the benign tumours of the stomach.

On examination of the literature available for the time being we found 24 cases of this type of invaginations of the stomach described in detail, viz.:

1. CHIARI, 1888 (see HENSCHEN): a woman, aged 44. — 2. COLLIER, 1896 (see HENSCHEN): a man, aged 21. — 3. MYER, 1913: a man, no age stated. — 4. WADE, 1913 (see FABRICIUS-MÖLLER and HENSCHEN): a woman, aged 48. — 5. BAYLAC-DIEULAFÉ, 1918 (see HENSCHEN): a woman, aged 43. — 6. DOEBLER, 1918: a man, aged 48. — 7. FABRICIUS-MÖLLER, 1918: a woman, aged 66. — 8. EUSTERMAN and SENTY, 1922 (see HENSCHEN and LÖNNERBLAD): a woman, aged 65. — 9. METAS, 1923 (see HENSCHEN and LÖNNERBLAD): a man, aged 55. — 10. BARNETT, 1925 (see HENSCHEN and LÖNNERBLAD): a woman, aged 54. — 11. MOUAT, 1925: a female, aged 12. — 12. GULEKE, 1927 (see HENSCHEN): a man, aged 32. — 13. SCHMIEDEN and WESTHUES, 1927 (see HENSCHEN): a woman, aged 78. — 14. HENSCHEN, 1927: a woman, aged 51. — 15. BOGORAS, 1930 (see LÖNNERBLAD): a woman, aged 42. — 16. SAUPE, 1932: a woman, aged 34. — 17. LÖNNERBLAD, 1933: a woman, aged 45. — 18. LÖNNERBLAD, 1933: a man, aged 54. — 19. JENSSEN, 1938: a woman, aged 46. — 20. JENSSEN, 1938: a man, aged 65. — 21. MEISSNER, 1939: a woman, aged 77. — 22. ZDANSKY, 1939: a woman, aged 57. — 23. HOYNINGEN-HUENE and ZIEGLER, 1940: a female, aged 16. — 24. ROTHE, 1941: a man, aged 59.

To these cases must be added our own, as No. 25, being that of a woman, aged 71.

No. 20 is the only case in which autopsy was not performed; it has, however, been included owing to the typical roentgen findings.

EUSTERMAN and SENTY have another case, that of a woman, aged 22 (quoted by HENSCHEN); but this case is excluded as the invagination was not proved, though probable. Otherwise LÖNNERBLAD mentions 4 cases which are either doubtful or not available in the literature. 3 Italian publications in which cases of gastro-duodenal invagination are said to be described (BONOMINI, 1937, BIGNAMI, 1939, and AGATI, 1940) have not been available either.

Out of regard to space we shall refrain from reporting each of the 24, often very interesting cases, but refer to the sources; here we shall give

a summary description of the facies morbi based on the knowledge of it which the 25 cases have given us.

The disorder is most frequently seen in elderly women. The primary abnormality which, as referred to above, is always the underlying cause of the occurrence of the invagination, was in all cases a tumour of the ventricle projecting into the lumen. This tumour has been stalky, except in No. 5 which was an intramural myoma, still projecting into the lumen. Only 3 out of the 25 tumours were malignant. No. 15 was a sarcoma fusi-cellular with a broad stalk and the size of a goose's egg (without any infiltration of the stomach wall worth mentioning); No. 7 was an adenopapilloma, the size of a hen's egg, showing doubtful signs of incipient malignity, and in No. 17 a fibroadenoma, the size of a pear, was found, it was excised but recurred later on. The tumour was benign in all the remaining 22 cases.

These findings are in conformity with the fact, which would also be expected, that a proper macroscopically demonstrable cancer does not give rise to invagination. For a stiff stomach wall, infiltrated with carcinoma, cannot be invaginated.

The 22 benign tumours (including No. 20) are of the following nature:

Adenopapillomata (fibroepitheliomata, fibroadenomata, polypi) were found in 15 cases. 10 of these were solitary (Nos. 8—11—12—13—14—16—18—20 (only roentgen diagnosis) 21—22), 1 multiple (No. 24), and 4 proved to be a great polypus or polypous mass in a diffuse adenopolyposis (Nos. 1—2—3 (luetic gastritis)—23).

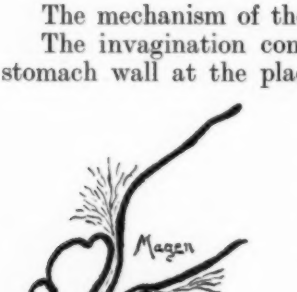
Myomata and fibromyomata were found in 6 cases (Nos. 4—5—6—8—10—25). *Fibroma* was seen in 1 case (No. 19). It was the size of a bean.

According to Fog-Möller, Henschen, Minnes and Geschickter, Myhre and Walton by far the greater part of benign tumours of the stomach are myomata and adenopapillomata, the former being in slight majority. When the ratio between myomata and adenopapillomata causing invagination in spite of this fact is 6 : 15, the cause is that only a small part of the myomata but most of the adenopapillomata project stalkily into the lumen, which is almost a condition of the occurrence of the invagination.

The size of the tumour differs from that of a pea (No. 12) to that of a goose's egg (Nos. 10—13—15—23), indeed in No. 3 a polypous mass larger than a fist was found. Most frequently the tumour is about the size of a hen's egg. The part of the stomach wall from which the tumour originated was in 16 cases (2/3 of all the cases) the canalis or antrum. This is in conformity with Henschen's statement that more than 2/3 of all benign tumours of the stomach are situated at the pylorus. In 7 cases the tumour originated somewhere in the corpus and in 2 cases from the fundus part.

The mechanism of the invagination is as follows:

The invagination commences with a tent-shaped retraction of the stomach wall at the place where the tumour is attached, the tumour being caught by the peristalsis (it may also be due to the weight of the tumour), and by means of the peristalsis the tumour now passes towards the pylorus and possibly through the latter, on into the intestinal canal forming the apex of the invagination; at the same time it drags a constantly increasing part of the stomach wall along. The invagination thus becomes total or circular after having been partial or lateral to begin with; in half the number of the cases it has been total or circular at some time. In 6 cases (Nos. 4—6—10—13—14—22) the intussusceptum has passed the whole of the duodenum and as far as 30 cm. into the jejunum (Nos. 4—14), while on the other hand in 2 cases (Nos. 12—21) the tumour only reached the pyloric ring. The intussusceptum being pushed into the duodenum the latter becomes distended and folded transversely whereby it is shortened.



Drawing according to LÖNNERBLAD.

The anatomical conditions described determine the roentgenogram characteristic of the disorder. The canalis part of the stomach is shortened (possibly completely effaced), and pointed like a cornet it may pass on into the bulbus with some longitudinal, convergent folds, which are caused by the longitudinally folded, invaginated part of the stomach. The duodenum is considerably distended with a central defective filling, originating from the intussusceptum with its tumour of the stomach, which may sometimes give the defective filling a peculiar relief, especially if the tumour is of polypous nature. Around the defective filling only a thin layer of contrast stuff is seen on the duodenal wall. This layer is arranged in concentric, ring-shaped stripes, concave towards the pylorus, which according to LÖNNERBLAD are due to the transversal folding of the duodenal sheath of the invagination above the intussusceptum already referred to (see the drawing), but which according to ZDANSKY should be due to the plicae Kerkringi. In our case the longitudinal and transversal folds referred to are seen in Fig. 1. Owing to the bulk of the intussusceptum the contrast medium may be pressed in between the outer and middle tubes of the invagination to the reduplication thus producing a characteristic collarshaped figure as in our case (see Fig. 1).

If the invagination is lateral this may be seen from a characteristic

defective filling, passing obliquely from one of the curvatures towards the pylorus.

14 cases were examined by means of roentgen rays while the invagination persisted (No. 4, however, only by means of transillumination). In Nos. 4—8—9—10—15 and 16 the findings were uncharacteristic and did not allow the diagnosis of invagination of the stomach to be established on the basis of the roentgen examination, nor could it be established on revision after post-mortem examination. In 6 cases (Nos. 17—18—20—22—24 and 25) the roentgen findings were typical as just described and thus the diagnosis was established. In 2 cases the roentgen diagnosis invagination of a tumour of the stomach only was established, in one of these cases (No. 19) the roentgen findings were, however, typical of a small lateral invagination.

The evacuation of the stomach differs with the highly varying degree of pyloric occlusion brought about by the invagination, from complete occlusion with retention of all the contrast medium in the stomach after 48 hours (No. 23), considerable retention (Nos. 10—15—17—18) to complete normal evacuation despite large central gastroduodenal invaginations (Nos. 9—24—22—25). In the remaining cases the conditions of the evacuation are not referred to.

The anatomicopathological alterations caused by the invagination are generally slight and without any great importance, as the stomach wall and its mesentery are jammed to a less degree (among other things owing to the great dilatability of the pyloric ring and the duodenum) and also because these parts are far more resistant than the intestinal wall and its mesentery.

The invaginated stomach wall may become oedematous and consequently somewhat stiff and small hemorrhages may be seen in the mucous membrane, but it is never gangrenous, still less detached. The invaginated tumour will frequently ulcerate and therefore give rise to hemorrhage, but as is known this will often be so in benign tumours of the stomach, which have not been incarcerated. In one case (No. 3) a part of an invaginated polypus, the size of a walnut, was detached, the invagination thus being obviated spontaneously.

Nor is the intussuscipiens generally injured. An exception is formed by No. 12 in which, after 5 days' invagination with total pyloric occlusion, a perforating peritonitis occurred as a consequence of a »dilatation necrosis» of the duodenal wall. In one case only (No. 6), where the patient died after 3 days' complete pyloric occlusion, adhesions were found between the serosa layers of the innermost and the next tube of the invagination, desinvagination thus being impossible post mortem.

In all the other cases that have been followed, desinvagination was possible. In 15 cases it was made in the course of operation, in 3 cases

post mortem (Nos. 1—7—21), and the remaining cases (Nos. 3—17—18—24 and 25) were desinvaginated spontaneously.

These cases of spontaneous desinvaginations are probably brought about by an increasing dilatation of the non-invaginated part of the stomach drawing the intussusceptum in the oral direction, partly by tiring and therefore relaxation of the spastically contracted muscles of the stomach and the duodenum, partly by the possible antiperistaltic movements of the duodenal sheath; lastly the constant vomiting by which the stomach so to speak is thrown to and fro may also contribute to the desinvagination. How readily invagination may alternate with desinvagination will appear from the fact that in 3 cases (Nos. 16—19 and 24) the invagination was seen to be developed during roentgen examination, and in case No. 14 the invagination was re-formed by gastric lavage after preceding spontaneous desinvagination. This lability highly influences

The Clinical Picture

Typical of the clinical picture of the disorder is first and foremost pyloric occlusion with violent pain in the epigastrium coming on more or less suddenly, often reminding of biliary colic, and persisting vomiting mixed with bile or blood. In the most marked cases ingestion of food is out of the question and the general health is influenced as in other forms of high ileus even to the extent of severe collapse and shock.

A typical complete occlusion of this nature was seen in 10 out of the 25 cases (Nos. 2—3—4—5—6—7—11—13—14—23). The invagination will often give rise to dilatation of the stomach and stenosis peristalsis (Nos. 1—3—6—7—8) and in most cases the invagination can be palpated as a tumour (Nos. 1—2—3—4—8—13—15—21—22) or only as an indefinite resistance (Nos. 14—16—18—23—25). As referred to above the case is often associated with hemorrhagic vomiting (1—3—6—9—10—17), melena or occult bleeding (Nos. 3—7—9—14—15—16—17—18—20—25), and the patients may be highly anemic.

A permanent complete pyloric occlusion may result in death in the course of a few days (Nos. 6 and 7), and in one case (No. 12) it caused perforation of the duodenum. In some cases (Nos. 1—8—9—15—18—21—24) the clinical symptoms of pyloric occlusion are less violent and more protracted, lasting for weeks or months (No. 1) possibly with periodical occurrence of the symptoms, according to whether the occlusion has been partial and possibly intermittent.

It is characteristic of the facies morbi that the actual case of invagination, i. e. the symptom complex leading to the diagnosis being established, is preceded by transient attacks of partial or total pyloric occlusion with

more or fewer of the above symptoms in a varying degree. This is distinctly so in 14 out of the 25 cases (Nos. 2—4—5—8—9—10—11—14—15—17—19—21—22—23). An especially peculiar feature is the finding of a palpable tumour, appearing and disappearing with the attacks (Nos. 4—10). These preceding attacks may have lasted for months or years (in No. 19 for 18 years), and their duration may be from minutes to several weeks. It cannot be decided whether they are due to slight cases of invagination or to incarceration alone, respectively prolapse, of the tumour of the stomach in the pyloric ring.

Characteristic of these preceding attacks is the strikingly rapid improvement of the general health after the acute symptoms of incarceration have ceased (CLARK NORMAN quoted by MEISSNER) and the often entirely free intervals between these (as for instance in Nos. 4—9—11—14—25). It is typical, too, that gradually the attacks increase in frequency and gravity, at last ending in the catastrophe which the case of actual invagination often is. Roughly, half the number of the cases take that course.

In 3 cases the actual invagination was not preceded at all by previous symptoms (Nos. 1—7 and 13 who all had pyloric occlusion).

In the remaining cases the incarceration of the tumour did not dominate the clinical picture, the symptoms were such as may otherwise be seen in benign tumours of the stomach (hemorrhage, loss of weight, dyspepsia).

Case No. 3, which is the only case in which the diagnosis was established on a purely clinical basis, deserves further reference despite the fact that this diagnosis is not quite unquestionable.

This was a case of adenopolyposis ventriculi, which gave the following symptoms: Achylia associated with a very copious production of mucus, hemorrhage from the mucous membrane, and once small polypous elements were found in the stomach sluicings.

A couple of years later an acute pyloric occlusion with gastric hemorrhage occurred, in association with marked stenosis peristalsis; as a tumour was felt in the pyloric region which on palpation gave the same sensation as fetal movements, the clinical diagnosis on invagination of the stomach with partial avulsion of an incarcerated polypus was established. 3 days later a polypous element, the size of a walnut, was found in the fæces, whereupon the symptoms subsided gradually.

Operation one year after in a symptom- free interval showed, besides diffuse polyposis, a racemose polypous paquet, 12 cm. long, at the greater curvature, 7 cm. from the pylorus. After this finding it cannot be wholly precluded that the pyloric occlusion the year before has been caused by a simple prolapse of the tumour through the pyloric ring only, and therefore the diagnosis of invagination of the stomach is not unquestionable, although probable.

Only in the above Case No. 3 the diagnosis was established exclusively on the clinical symptoms, and it was not quite justified. In 6 cases the diagnosis was established on the roentgenogram (Nos. 17—18—20—22—

24—25), while in Nos. 19 and 23 the diagnosis of invagination of a tumour of the stomach was established on the roentgenogram, the operation, however, showing that the stomach wall, too, was invaginated.

In 4 cases the diagnosis was only established on post-mortem examination (Nos. 1—6—7—21), while in the remaining cases it was established on operation. It will appear from this how difficult it is to diagnose this rare disorder.

When the actual invagination shows more or less marked symptoms of pyloric occlusion the picture may be mistaken for acute dilatation of the stomach, high ileus of another cause, or volvulus ventriculi (in which, however, a stomach tube can only be pushed as far as the cardia and therefore little or nothing of the stomach contents can be secured).

The erroneous diagnosis that is most likely to be established is that of ulcerated stenosing pyloric cancer, but against this speaks the gravity of the symptoms in connection with their short duration, the amazingly rapid restitution and the free intervals between the attacks, and their often periodical occurrence.

If, instead of showing acute symptoms, the actual invagination seems to be clinically identical with already existing symptoms of the underlying tumour, the invagination, like the preceding symptoms, will most frequently be mistaken for other disorders of the stomach.

As will be gathered from the picture of the symptoms described here the actual case of invagination will far from always require immediate operation, in numerous cases the patient's often highly exhausted general health can first be remedied and ought also to be so. But the patient should always be operated on, also in the cases where the invagination is spontaneously obviated, as the disorder has a marked tendency to recurrence. To this must be added that the tumour may also give rise to other fatal complications (especially malignant degeneration), for which reason it should always be removed.

The prognosis is rather serious, only about half the number of cases recovering. 19 out of the 25 patients were operated, 15 of them recovered as the underlying tumour was removed, 3 died in connection with the operation (Nos. 2—3—18), and in the 4th patient there was recurrence of the tumour (No. 17). 5 patients died without having been treated, 4 before the diagnosis was established, the 3 of the latter direct from the pyloric occlusion (Nos. 1—6—7), the fourth from intercurrent disease (No. 21), while the fifth, in whom the diagnosis was established in vivo, died from an intercurrent disease before the operation could be performed (No. 25). — One Case (No. 20) was not followed after the diagnosis had been established on the basis of the roentgenogram.

SUMMARY

A case of invagination of the stomach in a woman, aged 71, is reported. On roentgen examination an invagination ot the stomach was diagnosed, which on renewed roentgen examination 11 days after had disappeared; defective filling of the fundus was seen instead. The patient succumbed to a pneumonia. On post-mortem examination a stalky myoma, the size of a green walnut, was found in the fundus.

A brief reference is given to the different types of invagination of the stomach. In the available literature 24 cases of originally lateral, descending invaginations in non operated stomachs described in detail have been found and on the basis of these cases the facies morbi is gone through. The underlying cause of the occurrence of the invagination has in all cases been a tumour, which nearly always is benign and stalky. Based on the anatomical conditions the roentgen findings characteristic of the disorder are explained, by means of which it was possible in 6 (8) out of the 14 cases examined roentgenologically to establish the diagnosis of invagination of the stomach.

Spontaneous desinvagination is frequently seen, with subsequent re-invagination and this gives the typical facies morbi of attacks of pyloric occlusion.

ZUSAMMENFASSUNG

Über einen Fall von Invagination des Magens bei einer 71-jährigen Frau wird berichtet. Durch Röntgenuntersuchung wurde eine Mageninvagination festgestellt, die bei erneuter Röntgenuntersuchung 11 Tage später verschwunden war; statt dessen zeigte sich defekte Füllung des Fundus. Die Patientin starb an einer Pneumonie. Bei der Sektion fand man im Fundus ein gestieltes Myom von der Grösse einer grünen Walnuss.

Ein kurzes Referat über die verschiedenen Invaginationstypen des Magens wird gegeben. In der zugänglichen Literatur findet man 24 Fälle von ursprünglich lateralen, absteigenden Invaginationen in nichtoperierten Ventrikeln ausführlich beschrieben, und auf der Basis dieser Fälle wird das Krankheitsbild durchgenommen. Die zugrunde liegende Ursache des Vorkommens der Invagination ist in allen Fällen ein Tumor gewesen, der beinahe immer benign und gestielt war. An Hand der anatomischen Verhältnisse werden die für die Krankheit charakteristischen Röntgenbefunde erklärt, durch die es möglich war, bei 6 (8) Fällen von 14 röntgenologisch untersuchten Fällen die Diagnose Mageninvagination zu stellen.

Spontane Desinvagination kommt häufig vor, mit folgender Reinvagination und dieses ergibt das typische Krankheitsbild mit Anfällen von Pylorusverschluss.

RÉSUMÉ

Relation d'un cas d'invagination de l'estomac chez une femme de 71 ans. En l'examinant aux Rayons de Roentgen on diagnostique une invagination stomacale, laquelle avait disparu lors d'un nouvel examen radiologique 11 jours plus tard; à la place on voyait un défaut de remplissage du fundus. La malade succomba à une pneumonie. A l'autopsie on trouva un myome pédiculé, du volume d'une noix verte, dans le fundus.

Les différents types de l'invagination gastrique sont brièvement rappelés. Dans la littérature disponible on a trouvé la description détaillée de 24 cas d'invagination descendante, à point de départ latéral, dans des estomacs non opérés, et c'est à l'aide de ces cas qu'est brossé le tableau pathologique. Dans tous, la cause sous-jacente de l'invagination était l'existence d'une tumeur, presque toujours bénigne et pédiculée. C'est par la

rencontre de ces conditions que les auteurs expliquent les constatations radiologiques, caractéristiques de la maladie, et grâce auxquelles il a été possible d'établir le diagnostic d'invagination stomacale dans 6 (8) des 14 cas examinés aux Rayons de Roentgen.

Une désinvagination spontanée se voit fréquemment, avec une réinvagination suivante, et elle crée le tableau clinique typique des attaques d'occlusion pylorique.

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FROM THE ROENTGEN DEPT. OF THE KOMMUNEHOSPITALET, COPENHAGEN
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CASE OF CLEIDOCRANIAL DYSOSTOSIS[1]

by

Helge Eltorm

As cleidocranial dysostosis is a rare lesion it seemed appropriate to publish the following case since it is well-characterized and presents particular features that have been described but seldom. A brief report of the case was given in the Danish Radiological Society, in spring 1944. Like most of the cases published, this too was discovered accidentally.

The patient is a woman, married, 52 years old, measuring 143 cm. in height and weighing 50 kg. She has been well in childhood, especially she claims not to have had rickets. 15 years ago she was operated on for inguinal hernia, and the same operation has been repeated twice since. The menses were regular from the age of 18, of normal intensity and duration, with intervals of 28 days. In 1943 uterine curettage was performed because of climacteric bleeding. She was readmitted to hospital in 1944 because of facial paralysis and metrorrhagia. During one of her stays in the hospital for operation for the hernia, on roentgen examination it was discovered accidentally that the patient had bilateral congenital coxa vara, but otherwise her illness has not been recognized on any hospitalization before the last one.

She was married at the age of 27, and 2 years later she gave birth to a normal boy by natural delivery. There has been no parturition or abortion since (contraception employed). The patient has always been small and obese, with very slanting shoulders, but she has been able to do her work normally; in particular she has always been a good walker, and just recently she has become a little stiff in the hip-joints. She has noticed herself that her shoulders are somewhat abnormal, in particular in the respect that she was able to bring the shoulders so far anteriorly that they could touch each other. She has not attached any particular significance to this because her mother presented the same abnormality. Otherwise no instances of the anomaly is known to have occurred in the family. The patient has had a full dental prothesis since the age of 16. At her last hospitalization, in 1944, for facial paralysis — in the Ear Clinic of the Kommune Hospital — roentgen examination of the skull was performed, and this revealed the large defect anteriorly in the skull, together with the Wormian bones in the posterior cranial fossa. Further roentgenography of the entire osseous system disclosed the bone changes characteristics of cleidocranial dysostosis complicated by several other defects occurring now and then in this lesion.

[1] Submitted for publication, Aug. 24, 1944.

On physical examination the patient was found to be a little obese. She is a little moody but generally cheerful. Her intelligence is judged to be normal. Her skull is broad, resembling mostly that of a »square head». The distance between the eyes is strikingly large. Anteriorly on the skull a depression can be made out, about 3—4 cm. wide and reaching from a couple of cm. above the glabella to about 3—4 cm. posteriorly to the coronal suture and extending about 2—3 cm. to either side along this suture. The flow of this depression is hard and fibrous; no pulsation is felt.

As mentioned, the patient has a full dental prothesis, and on further questioning she states that she has never had a change of teeth, the milk teeth falling out gradually during puberty. Otherwise the head presents no abnormality besides peripheral facial paralysis of the right side.

Fig. 1.

The neck is normal, but the shoulders are strikingly slanting, and they can be brought so far anteriorly as almost to touch each other (Fig. 1). Palpation reveals that the greater part of both clavicles is missing; only the end of each clavicle is felt as a small movable, about 2—3 cm. long, prominence anteriorly on the acromion, pointing medially and another prominence, about 4—5 cm. in length on the upper lateral corner of the sternum, pointing laterally. The mobility in the shoulder joints is normal. Palpation of the elbow-joints shows bilateral absence of the lateral epicondyle of the humerus, resulting in a pseudosubluxation of the radius and abnormally great pronation. Otherwise the movements in the joints are normal. There is a pronounced bilateral brachyphalangia; nails normal.

The thorax is strikingly narrow above. There is a considerable hypertrophy of the breasts. Auscultation of the heart and lungs: No abnormality.

Abdomen: Normal findings.

The lower extremities look normal. On both sides the trochanter is elevated 3—4 cm. and there is a slight reduction in the mobility in the hip-joints in all directions, though especially abduction. Apart from brachyphalangia on both feet, the lower extremities are otherwise normal.

The roentgen picture of the *skull* (Figs. 2—3) shows a defect in the ossification of the theca, commencing anteriorly in the midline a couple of centimeters above the glabella. This defect is narrow anteriorly, widening gradually and symmetrically and then narrowing again a little anteriorly to the coronal suture; but corresponding to this suture the defect widens again, becoming 6 cm. wide, whereafter it stops rather abruptly. The rest of the theca is thick-walled. The occipital bone is divided into many small parts separated by distinct sutures. Both ear regions are very massive, without pneumatization. The entire cranial base appears rather short. Sutures and vascular grooves normal. Frontal sinuses aplastic, but maxillary sinuses and ethmoidal cells normal.

The upper and the lower jaws are rather poorly developed and contain a number of retained teeth, probably all the permanent teeth, which are quite undeveloped. There is no prognathism.

The *cervical vertebral column* shows spina bifida corresponding to the lower 3—4 vertebrae, and involving also the 2—3 upper thoracic vertebrae (Fig. 4). The transverse processes of the 7′ cervical vertebrae are 2—3 cm. long, resembling cervical ribs.

Fig. 2.

Fig. 3.

Fig. 4.

Fig. 5.

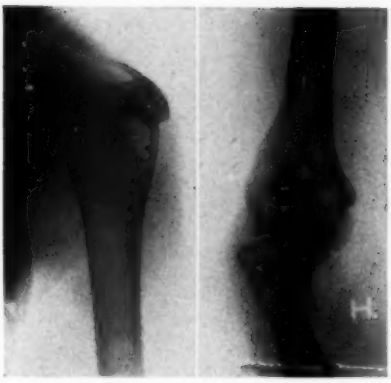

Fig. 6.

Fig. 7.

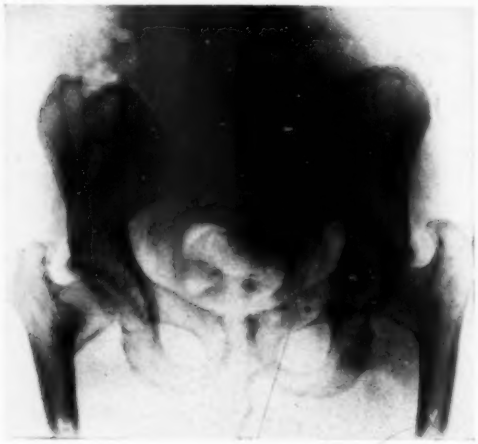

Fig. 8.

All the *thoracic vertebrae* present »inversely wedge-shaped» bodies, being of normal height anteriorly but narrowing considerably posteriorly because the ossification of the margin of the body posteriorly is defective. The center of ossification is seen distinctly in nearly all the bodies. Otherwise this part of the column appears normal except for a slight degree of sinistroconvex scoliosis (Figs. 4—5).

The *ribs* are markedly slanting but present no other abnormality (Fig. 4). The sternum appears normal.

The *clavicles* are markedly defective. Of the sternal parts only a couple of rudimentary remnants are seen, measuring about 4—5 cm. in length, and projecting laterally in normal direction. The acromial ends of these bones are represented merely by a couple of small pointed bones, about 2 cm. in lentgh, which appear to continue towards the sternal ends of the clavicles as a fibrous cord (Figs. 4 and 6).

The *scapulae* are small and the glenoid cavity is poorly developed. The coracoid process is small and apparently malformed. (Figs. 4 and 6).

In the *humerus*, on both sides, the lateral part of the epicondyle is missing together with the capitulum, so that the head of the radius appears to be subluxated. Under the medial epicondyle a bony prominence is seen to project just as far out as the epicondyle (Fig. 7).

In the *pelvis*, on both sides, the ilium is defectively developed, while the other pelvic bones are normal. The acetabulum is flat and very oblique. The symphysis is wide, but it is doubtful whether the fusion is defective. The sacrum is normal (Fig. 8).

The *femur*, on both sides, shows pronounced congenital coxa vara. The neck arises at the level of the lesser trochanter, making thus the greater trochanter appear very large. No head is seen on either side, but the ends of the neck are rounded and resemble a head. The joint gap is normal. (Fig. 8).

The remaining part of the lower extremity presents no abnormality beyond brachyphalangia of the toes.

Summarizing the roentgen findings, then, we here meet with:

1) defects in the theca of the skull;
2) Wormian bones in the occipital bone;
3) sclerosis of the petrous portion;
4) aplasia of the pneumatic spaces in the temporal and frontal bones;
5) small upper and lower jaws;
6) total retention of the permanent teeth;
7) spina bifida in the cervical and thoracic columns;
8) excessively developed transverse processes of the 7' cervical rib;
9) markedly defective clavicles;
10) defective development of the scapulae, with defective coronoid process and glenoid cavity;
11) aplasia of the medial epicondyle and capitulum of the humerus;
12) brachyphalangia;
13) defective development of the iliac bone with poor development of the acetabulum on both sides;
14) split pelvis (?);
15) bilateral congenital coxa vara.

The first case of cleidocranial dysostosis described dates back to 1765 when MARTIN described a case of congenital defect of the clavicle. In 1871 SCHEUTHAUER reported as the first that the clavicular defect is associated with abnormal ossification of the skull, but it was P. MARIE & SAINTON who in 1898, independently of SCHEUTHAUER again pointed out the simultaneous bony fects and their hereditary aspects. These authors described the affection thoroughly and gave it its present name. Among other things they also mentioned the abnormal dentition. In 1912 PALTAUF described the gap in the symphysis associated with cleidocranial dysostosis; and in 1921 JANSEN pointed out that the lesion ought to be associated with brachyphalangia.

Besides these anomalies many others have been described, as the more important of which the following may be mentioned: cervical ribs, spina bifida, congenital clubfoot, congenital coxa vara, subluxation of the radius, malformation of the fingers, defects of the scapula, incomplete ossification of the sternum and sacrum, laxity of joints, synostosis between the cervical vertebrae, drumstick nails, congenital dislocation of the hip and asymmetry of the face.

As probably secondary phenomena there may be various muscular anomalies, most frequently grouped around the bones in the shoulder.

The lesion has been described very thoroughly by HULTKRANZ in a monograph of 1908. In this country KRABBE & FOGED (1924) reported a case that was complicated by increased metabolism. In 1937 VALENTIN gave a good description of the lesion and its genetic aspects. Also this

author has given a rather comprehensive list of references. So I shall not here enter further into the literature but refer the reader to the works mentioned.

In 1924 KRABBE & FOGED thought that altogether about 100 cases of this affection had been published. The present number will probably lie between 150 and 200.

As to the *pathogenesis*, this question has been investigated very thoroughly by HULTKRANZ (1908) and BAUER (1928). The latter thinks that the anomalies may be expected anywhere in the mesenchymal tissue.

The *etiology* has been discussed ardently by many authors including entirely speculative statements, theories about amniotic pressure and theories about infection. On the other hand, all the authors agree on the unquestionable inheritance of the lesion. Among others, ASCHER & ENGELMANN (1928) have described 26 families with this affection. As to this question the reader is referred to BAUER and the other above-mentioned authors. BAUER thinks that the lesion must be due to a mutation which electively involves the total preformed osseous system.

VALENTIN reckons with 4 *cardinal symptoms* of the affection:

1) unilateral or bilateral aplasia of the clavicle;
2) anomalies in the ossification of the skull and the dental system;
3) anomalies in the pelvis and proximal part of the femur;
4) anomalies of the fingers and toes.

As will be noticed, all these four symptoms are observed in a marked degree in the present case, which further presents most of the additional anomalies that may be associated with the disease — even several of the more rare ones. In addition, this patient presents a change which, as far as I know, has not been described previously, namely: the defective ossification of the marginal edges of the bodies of the thoracic vertebrae. The subluxation of the radius demonstrated in this case has been described previously by RAUBITSCHEKS in 1915 — which, as far as I have been able to find out, is the only instance of this complication reported previously. Also the scapular deformities are rare.

SUMMARY

Report is given of an accidentally discovered instance of cleidocranial dysostosis in a woman, 52 years old, whose mother had the same affection. This patient presents all the typical changes occurring in this affection in a pronounced degree. In addition, there is defective ossification of the marginal edges of the bodies of the thoracic vertebrae. Furthermore, this patient presents a bilateral subluxation of the radius due to defective development of the capitulum and lateral epicondyle of the humerus.

The etiology and pathogenesis are mentioned briefly together with the genetic aspects of the affection, the reader being referred to previous works for a comprehensive review of the literature.

ZUSAMMENFASSUNG

Es wird über einen zufällig entdeckten Fall von kleidokranialer Dysostose bei einer 52jährigen Frau berichtet, deren Mutter den gleichen Zustand aufwies. Diese Patientin zeigt in ausgesprochenem Grade alle die bei dieser Krankheit vorkommenden typischen Veränderungen. Ausserdem liegt defekte Verknöcherung der marginalen Ränder der Brustwirbelkörper vor. Darüber hinaus zeigt die Patientin noch eine bilaterale Subluxation des Radius, bedingt durch defekte Entwicklung des Capitulum und des lateralen Epicondylus des Oberarmknochens.

Die Ätiologie und Pathogenese werden kurz erwähnt, sowie auch die genetischen Faktoren des Leidens, wobei für eine ausführliche Übersicht des Schrifttums auf frühere Arbeiten verwiesen wird.

RÉSUMÉ

Relation d'un cas de dysostose cléido-cranienne découvert fortuitement chez une femme de 52 ans dont la mère souffrait de la même affection. La malade présente, à un degré prononcé, toutes les altérations typiques qu'on rencontre dans cette entité morbide. En plus, on trouve chez elle une ossification incomplète des bords marginaux des corps vertébraux thoraciques. Outre cela elle est atteinte d'une subluxation bilatérale du radius, due au développement défectueux des têtes radiales et des épicondyles huméraux.

L'étiologie et la pathogénie sont brièvement esquissées, ainsi que les aspects génétiques de l'affection, le lecteur étant au surplus renvoyé à des travaux antérieurs où il trouvera une bibliographie complète.

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LE FORAGE DE L'EPIPHYSE FÉMORALE DE DUVERNAY[1]

Un examen complémentaire de 41 cas

par

Jørgen Ernst

Le traitement de l'arthrosis coxae au moyen de forage a été exécuté, pour la première fois, par AIMES et REYNES. Pourtant ce fut spécialement LOUIS DUVERNAY qui, en 1930, a mis au point la méthode, raison pour laquelle celle-ci porte son nom. Le traitement fut, pour la première fois, décrit par son successeur J. GRABER-DUVERNAY en 1932 (4). Au moyen d'un perforateur de 6 millimètres de diamètre on fore un canal à travers le collum et le caput femoris. Au début, on introduisait d'ordinaire une cheville d'os mort dans ce canal, mais on essayait vite de s'en passer, sans que cela n'ait influencé l'efficacité du traitement. HYBBINETTE (9) a modifié l'opération de cette manière que, au lieu d'exécuter le forage avec un perforateur de 6 millimètres, il a foré 8—12 canaux avec un perforateur de 3 millimètres. La plupart des auteurs affirment que la disparition des douleurs — éventuellement une amélioration — se produit immédiatement, tandis que HYBBINETTE remarque par exemple que le processus d'amélioration peut mettre jusqu'à un an pour se développer.

Les explications du mode d'action de l'opération ont été très contradictoires. GRABER-DUVERNAY (4) a affirmé, avec l'appui de LERICHE et POLICARD (11 & 12), que le forage a causé une diminution de l'hyperémie de l'os qui avait conditionné la raréfaction osseuse. Il a basé sa conception sur des recherches oscillométriques d'où il avait constaté que la jambe malade montrait, avant l'opération, la plus grande courbe. Pendant les premières semaines après l'intervention, la courbe augmentait ultérieurement et tombait ensuite pour atteindre un niveau inférieur à celui enregistré avant l'opération. Au côté sain il a en outre constaté,

[1] Remis à la Réd. le 24 Août 1944.

en corollaire de l'opération, un abaissement oscillométrique qui disparaissait lentement. D'autres auteurs, tels que HYBBINETTE (9) et HACKENBROCH (8), comprennent tout au contraire l'effet comme une hyperémie qui cause des granulations fraîches et des modifications de la structure de l'os, c'est-à-dire plutôt quelque chose comme le forage en cas de pseudoarthroses selon la méthode de Beck.

Dans le premier compte rendu de GRABER-DUVERNAY (4) sont mentionnés 10 cas dans lesquels on a pratiqué le forage avec un bon résultat. Dans un bulletin (5) 3 ans plus tard, il indique que sur ces 10 cas 6 sont bons encore — c'est-à-dire 60 % pendant plus de 3 ans. Dans une nouvelle série de 14 cas, 60 % également sont bons. En 1937, RÉNÉ et GASTON CHARRY (3) ont mentionné 8 cas d'arthrosis deformans qui avaient tous été forés avec un bon résultat. HAMANT et GIRARD (6) ont 5 patients dont 6 hanches furent forées, 4 avec un bon résultat. En 1938, PADOVANI (14) a rendu compte de 16 cas, dont 4 seulement étaient décidément bons et 2 améliorés qu'il n'a cependant pas osé attribuer, avec certitude, à la méthode. Du côté de l'Allemagne, je n'ai trouvé qu'un rapport de HACKENBROCH (7) qui dans 6 cas a constaté un bon résultat chez tous — pourtant la durée de l'observation n'a été qu'un an. Du côté de la Suède, HYBBINETTE (9) a, en 1935, sur la base de sa modification spéciale de la méthode, rendu compte de 11 cas dont 10 étaient bons. L'année suivante, son élève LIDSTRÖM (13) a recueilli 41 cas dont 4 seulement semblent mauvais. Cependant, rien n'est indiqué au sujet de la période d'observation. Du côté du Danemark ce fut, comme on sait, AAGE BERNTSEN qui en 1936 (1) a préconisé la méthode. En 1939 (2), il a fait le bilan de ses matériaux. Sur 13 patients observés pendant une année, 76.9 % montraient une amélioration, et sur 22 patients observés pendant 2 ans, 56 % étaient améliorés. Somme toute, sur 35 patients observés au cours d'une année, 59.8 % montraient une amélioration — soit environ 60 %. En 1943, LEHMANN (10) en établissant le bilan des matériaux de l'hôpital orthopédique a constaté 61 % d'améliorations sur 82 cas observés pendant 6 mois, et après 4—8 ans le chiffre des améliorations était 46 %.

Si difficiles qu'ils soient à comparer — soit parce que la durée de la période d'observation varie, soit, dans certains cas, parce que la durée de cette période n'pas été indiquée — les résultats diffèrent donc dans une assez grande mesure. Par conséquent, l'idée s'impose de chercher à éclaircir cette différence, éventuellement par des indications ou contre-indications particulières. GRABER-DUVERNAY (5) mentionne comme contre-indication entre autres choses l'obésité, tandis que BERNTSEN (2) affirme que ni sexe, âge, obésité, caractère bilatérale ni contracture ne sont des contre-indications. HAMANT et GIRARD (6) conseillent de n'avoir recours à l'intervention que dans des cas frais avec une bonne motilité.

HYBBINETTE (9) indique au point de vue purement anatomo-pathologique deux formes: 1) un type scléro-ostéophytique avec des ostéophytes fermes. Le tissu osseux partiellement sclérotique et partiellement avec des kystes le plus souvent entourés d'une zone sclérotique. Au point de vue clinique, ce type révèle un développement très lent, et la limitation de motilité était plus apparente que les douleurs. 2) un type qui présente des altérations atrophiques et raréfiantes et dont les néoproductions ostéophytiques sont molles, la raréfaction osseuse et les formations de kystes prononcées; ces derniers ne sont pas, contrairement à la première catégorie, entourés d'un tissu sclérotique. Ces kystes rend l'os mou et compressible. Au point de vue clinique, ce type est caractérisé par un développement rapide et beaucoup de douleurs — même en repos. Il est d'avis que c'est justement ce type qui est propre au forage. HACKENBROCH (8) trouve également que ce sont justement les cas caractérisés par kystes et raréfaction osseuse qui se prêtent au forage, mais il souligne en outre que dans les cas où il est aussi question de kystes et de raréfaction osseuse dans l'acetabulum, il faut — en dehors de forage du col fémorale — procéder à l'introduction de clous dans l'acetabulum ce qui a le même effet biologique. Dans les cas où les douleurs sont principalement dues à une mauvaise statique dans l'articulation coxo-fémorale ayant pour corollaire une charge abnorme des mucles ou des altérations considérables du cartilage articulaire, l'effet du forage est nul ou, en tout cas, douteux. Au moyen d'une analyse des radiogrammes de 66 patients, LEHMANN (10) a cherché à trouver des indications et contre-indications pour l'opération. Il y a une petite prédominance quant à la formation de kystes pour les résultats cliniquement favorables et une petite prépondérance presque analogue pour un fort rétrécissement de la fente articulaire quant aux résultats cliniquement mauvais, mais la différence est trop petite pour servir de base à des constatations quelconques, et il en conclut que l'examen radiologique ne permet pas de constater quels sont les cas qui seront propres à l'opération. Il trouve, cependant, que les cas qui sont secondaires, par exemple par rapport à la luxation incomplète congenitale, au décollement épiphysaire ou Morbus Calvé-Perthe, ont une meilleure prognose que les cas idiopathiques primaires. LEHMANN n'a dont pas réussi à confirmer, par voie radiologique, l'importance des formes anatomo-pathologiques de HYBBINETTE pour la prognose de l'inforatio colli femoris.

Propres recherches

A l'hôpital de Svendborg on a, pendant la période 1936—1944, exécuté le forage du col fémoral 41 fois chez 39 patients, deux patients ayant été traités dans les deux hanches. La technique a dans l'essentiel

été celle indiquée par BERNTSEN (1). On s'est servi d'un perforateur de 5 millimètres de diamètre, et dans la plupart des cas on a foré plusieurs canaux — soit jusqu'à 8, le plus souvent toutefois 3—4. Chez un patient il n'y a eu qu'un seul canal de forage. De ces 41 cas j'ai personnellement fait des examens complémentaires au sujet de 32, dont 23 ont été radiographiés pour contrôle. De 7 patients j'ai obtenu des renseignements écrits sur leur état, et ce ne sont que 2 patients que je n'ai pas pu suivre, puisqu'un mourut, et actuellement je ne pouvais pas venir en contact avec l'autre à cause d'un Encephalitis letargica. Cependant, le journal d'une hospitalisation quelques ans après l'opération contient l'information qu'il était sans douleurs, en tout cas 3 ans après l'intervention.

Des 41 cas, 19 étaient femmes et 22 hommes. 25 étaient du côté droit et 16 du côté gauche. L'âge au moment de l'opération résulte de la table 1.

Table 1

Âge au moment de l'opération

31—40 ans	3
41—50 »	6
51—60 »	19
61—70 »	11
71—80 »	2
	41

La durée des symptômes avant l'opération résulte de la table 2; c'est-à-dire que 23 des patients ont eu les symptômes plus de 5 ans avant l'opération.

Table 2

Durée des symptômes avant l'opération

<1 an	3	5—10 ans	12
1—2 ans	4	10—15 »	3
2—3 »	5	15—20 »	6
3—4 »	3	20—30 »	1
4—5 »	3	> 30 »	1

Sur les 41 cas, 33 étaient idiopathiques primaires et 8 étaient secondaires, à savoir 5 après contusions de la hanche, 1 après fract. colli femoris, 1 après subluxatio congenita et 1 après coxa vara.

Sur les 41 cas, 15 n'avaient pas été traités auparavant. 18 avaient reçu un traitement physiothérapique, 3 avaient été traités par radiothérapie, 3 par physiothérapie et radiothérapie, 1 par physiothérapie, radiothérapie et l'opération Camitz, et 1 a subi un traitement d'injection.

Après l'opération, il y avait deux cas d'hématome dans la blessure, en deux cas phlebitis, dans un cas pneunomie et dans un cas une parésie Peroneus. Chez 4 patients on a, simultanément avec l'opération (ou à

quelques jours d'intervalle), procédé a une ténotomie des adducteurs à cause d'une contracture de ceux-ci.

Les résultats du traitement ressortent de la table 3.

Table 3

Résultats du traitement

	Juste après l'op.		6 mois après l'op.		2 ans après l'op.		6 ans après l'op.	
Indolore	30=73.2 %	90.2 %	24=63.2 %	76.4 %	22=59.4 %	70.1 %	15=53.6 %	64.3 %
Amélior.	7=17 %		5=13.2 %		3= 8 %		2= 7.1 %	
Patient No. 35	1= 2.5 %	9.8 %	1= 2.6 %	23.6 %	1= 2.7 %	29.9 %	1= 3.6 %	35.7 %
Inchangé	3= 7.3 %		8=21 %		11=29.9 %		10=35.7 %	
Pas compris dans le calcul			3 No. 38, 11, 29		4 No. 14		13 No. 5, 8, 15, 19, 20, 21, 24 b, 32 et 39	

Le patient No. 38 est mort, et tous renseignements sur le développement après l'opération font défaut. Les patients No. 11 et 29 n'ont été observés que pendant 3 mois, raison pour laquelle il faut les omettre dans le calcul du résultat 6 mois après l'opération. Le patient No. 14 n'a été observé que pendant 6 mois, et il faut donc l'omettre dans la rubrique: 2 ans après l'opération. Les patients No. 5, 8, 15, 19, 20, 21 et 24 b n'ont été observés que pendant respectivement 2, 4, 5, 2, 2, 2, et 3 ans après l'opération. Le patient No. 32 est mort 2 ans après l'intervention, et le patient No. 39 était celui avec encephalitis letargica mentionné ci-dessus; pour cette raison, il n'entre pas en ligne de compte dans le calcul des résultats 6 ans après l'opération.

Enfin, en ce qui concerne le patient No. 35, je remarque que ces douleurs n'ont disparu qu'un an après l'opération, et ensuite il a été indolore pendant 5 ans et est toujours exempt de symptômes. Conformément à la conception de HYBBINETTE (9), il est possible que le processus d'ossification ait mis un an à s'achever, mais comme je n'ai pas osé dire avec certitude propter ou post, j'ai consacré une rubrique spéciale à ce patient. Pour ce qui concerne 3—4 des autres patients, l'amélioration ne s'est pas non plus produite immédiatement, ainsi qu'ont affirmé la plupart des autres auteurs, mais par degrés au cours de 2—3 mois.

En comparant ces chiffres avec ceux de BERNTSEN et de LEHMANN, on constate que les résultats de l'hôpital de Svendborg sont un peu meilleurs; si l'on regarde tout particulièrement la longue période d'observation, la différence est grande. LEHMANN (10) avait, après 4—8 ans d'observation, 46 % d'améliorations, tandis que nous en avons 64 % au bout de 6 ans.

Cela serait d'un grand intérêt si, à la base des matériaux recueillis on pouvait tracer certaines lignes de conduite quant à l'indication pour

le forage du col fémoral. C'est pourquoi j'ai ci-dessous traité mes matériaux de cette fin.

HAMANT et GIRARD (6) ont conseillé de ne procéder à l'opération que dans les cas frais avec une bonne motilité. Comme mentionné, 18 de nos patients avaient eu leurs symptômes 5 ans ou au-dessous avant l'opération, et 23 patients plus de 5 ans. L'examen des 37 patients qui ont été observés pendant 2 ans donne le résultat suivant:

Table 4

La prognose par rapport à la durée des symptômes avant l'opération

	Cliniquement bons	Cliniquement mauvais
< 5 ans	11	6
> 5 »	15	5
	26	11

Il n'y a donc aucune différence entre ces deux groupes.

Chez 28 des patients qui ont été observés pendant 2 ans ou plus j'ai fait un examen complémentaire quant à la motilité dans l'articulation coxo-fémorale. Sur ces 28 cas j'ai constaté une diminution des douleurs chez 19, tandis que 9 étaient inchangés. Avant l'opération et à l'examen postérieur, la motilité était telle qu'elle résulte de la table 5:

Table 5

La motilité avant l'opération et à l'examen complémentaire

	Avant l'opération			À l'examen compl.	
19 Cliniquement améliorés	Bonne ..... 1 Presque bonne..... 8	48 %		Meilleure..... Inchangée	37 %
	Légèrement limitée.. 4 Fortement » .. 6	52 %		Légèrement aggravée .. Aggravée.....	63 %
9 Cliniquement inchangés	Bonne ..... 0 Presque bonne..... 3	33 %		Meilleure..... Inchangée	env. 10 %
	Légèrement limitée.. 2 Fortement » .. 4	66 %		Légèrement aggravée Aggravée.....	» 90 %

La motilité avant l'opération est peut-être un peu meilleure dans le groupe cliniquement bon que dans les cas cliniquement mauvais, mais il n'y a pas de différence sûre. A l'examen complémentaire, par contre, il y a une différence nette puisque, dans le groupe cliniquement bon, il y a une aggravation de la motilité chez 63 % des patients contre 90 %

dans le groupe cliniquement mauvais. Dans le premier groupe, il se trouve 1 patient avec une ankylose complète contre 3 patients dans le groupe cliniquement mauvais.

LEHMANN (10) a souligné que la prognose est la meilleure pour les patients chez lesquels l'arthrose est secondaire par rapport à des anciennes affections coxo-fémorales, comme par exemple le décollement épiphysaire ou la maladie Calvé-Perthe. Comme mentionné ci-haut, l'affection était secondaire chez 8 de mes patients. Les 3 patients avec fract. colli femoris, subluxatio congenita et coxa vara, ainsi que 3 des 5 patients avec contusions étaient cliniquement bons, et 2 seulement étaient cliniquement mauvais, mais les chiffres sont trop petits pour permettre d'établir le pourcentage.

Enfin, en ce qui concerne l'examen radiologique, j'ai examiné, premièrement si l'on peut — ainsi que LEHMANN (10) a essayé — faire la prognose pour l'opération sur la base du radiogramme pris avant celle-ci, et deuxièmement si l'on pouvait, éventuellement par voie de radiologie, confirmer la classification anatomo-pathologique de HYBBINETTE (9). En conséquence, j'ai partiellement fait une estimation des radiogrammes avant l'opération en attachant spécialement de l'importance à la différence entre le côté sain et le coté malade, et partiellement comparé les radiogrammes pris avant l'opération à ceux obtenus à l'examen complémentaire. Le nombre des patients observés pendant 2 ans est, comme déjà mentionné, 37; il y a donc 37 radiogrammes dans le premier groupe, soit 26 cliniquement bons et 11 cliniquement mauvais. Sur ces 37 cas, 21 seulement ont été radiographiés pour contrôle, raison pour laquelle le deuxième groupe ne comprend que 21 radiogrammes. Les résultats ressortent des tables 6 et 7.

Table 6

Examen radiologique avant l'opération

Degré du changement	Kystes dans le caput		Kystes dans l'acetabulum		Raréfaction osseuse		Éburnation		Ostéophytes		Déformation de la tête articulaire		Rétrécissement de la fente articulaire		Luxation incomplète	
	c l i n i q u e m e n t															
	bon	mauv.	bon	m.	b.	m.	b.	m.	b.	m.	b.	m.	b.	m.	b.	m.
+ +	58	45	11	27	50	27	19	64	58	27	31	16	46	55	11	36
+	42	55	39	27	39	46	54	36	31	46	27	16	16	36		
(+)											31	52	27	9		
0			50	46	11	27	27		11	27	11	16	11		89	64

Les chiffres sont en pourcent

Table 7

Résultat radiologique avant l'opération et à l'examen complémentaire

	Kystes dans le caput		Kystes dans l'acetabulum		Raréfaction osseuse		Éburnation		Ostéophytes		Déformation de la tête articulaire		Rétrécissement de la fente articulaire		Luxation incomplète	
	c l i n i q u e m e n t															
	bon	mauv.	b.	m.	b.	m.	b.	m.	b.	m.	b.	m.	b.	m.	b.	m.
Constaté avant l'opération ...	12	9	8	7	11	7	9	9	12	9	11	9	11	9	2	2
À l'examen complémentaire:																
Augmenté ...		6		3		5	9	2	10	4	4	5	8	6	1	1
Inchangé.....	2	1	1	2		1		2	2	5	7	4	3	3	1	1
Diminué	10	2	7	2	11	1		5								

De la table 6 il résulte que chez la plupart des patients il y avait des kystes dans le caput, bien que ceux-ci apparaissent dans une plus grande mesure dans le groupe cliniquement bon. Les kystes dans l'acetabulum n'ont été trouvés que chez 50 % environ et, en conséquence, ils ne jouent guère un rôle si important que les kystes dans le caput. Dans le groupe cliniquement bon, la raréfaction osseuse ne fait défaut que dans $^1/_8$ des cas contre $^1/_4$ dans le groupe cliniquement mauvais, de même que la raréfaction osseuse est aussi plus marquée dans le groupe cliniquement bon que dans l'autre groupe. En ce qui concerne l'éburnation, les chiffres sont proportionnellement inverses. Ici l'éburnation fait défaut chez env. $^1/_4$ dans le groupe cliniquement bon par contraste avec le groupe mauvais, où l'éburnation se manifeste dans tous les cas — de même que celle-ci est aussi plus marquée que dans le groupe cliniquement bon. Quant aux néo-productions ostéophytiques, celles-ci semblent se présenter les plus grandes et le plus souvent dans le groupe cliniquement bon. La déformation de la tête articulaire semble paraître avec presque la même fréquence dans tous les deux groupes, mais peut-être un peu plus prononcée dans le groupe cliniquement bon que dans l'autre groupe. Inversement, le rétrécissement de la fente articulaire se présente plus souvent et le plus fortement dans le groupe cliniquement mauvais. Enfin il y a un peu plus de cas de luxation incomplète dans le groupe cliniquement mauvais que dans l'autre catégorie.

Les différences entre les groupes ne sont donc pas grandes et décisives, mais tout de même la tendance va un peu dans la direction de la classification de HYBBINETTE, c'est-à-dire les grands kystes avec une raré-

Fig. 1 a.

Fig. 1 b.

Fig. 2 a.

Fig. 2 b.

faction osseuse prononcée et une éburnation faible sont propres au forage, et les kystes entourés d'un tissu éburnisé et avec une raréfaction osseuse faible ou sans une telle ne se prêtent pas au forage.

Il résulte de la table 7 que les kystes et la raréfaction osseuse s'affaissent dans le groupe cliniquement bon pour être remplacés par un tissu éburnisé par contraste avec le groupe cliniquement mauvais, ou il y a souvent une augmentation des kystes et de la raréfaction osseuse et fréquemment une diminution analogue de l'éburnation. Dans aucun

Fig. 3 a.

Fig. 3 b.

Fig. 4 a.

Fig. 4 b.

des groupes il n'y a une diminution des néo-productions ostéophytiques et de la déformation de la tête articulaire, ni du rétrécissement de la fente articulaire ni de la luxation incomplète; tout cela semble, d'une façon générale, ou bien rester inchangé ou bien s'augmenter.

L'examen complémentaire des patients traités par forage montre donc plus clairement qu'il résulte des premiers radiogrammes seuls, qu'il existe une différence susceptible d'être prouvée par voie radiologique entre les cas cliniquement bons et cliniquement mauvais et, dans les grands traits, l'examen radiologique confirme donc la classification

Fig. 5 a.

Fig. 5 b.

Fig. 6 a.

Fig. 6 b.

de HYBBINETTE dans un type scléro-ostéophytique et un type avec des altérations atrophiques et raréfiantes.

Sur les figures 1—4 sont montrés 4 cas de hanches cliniquement bonnes, où les kystes et la raréfaction osseuse ont diminué en étant remplacés par un tissu éburnisé. Les figures 5—6 montrent deux cas de hanches cliniquement mauvaises, où les kystes et la raréfaction osseuse ont augmenté et l'éburnation a diminué. Sur les figures, a) sont les radiogrammes pris avant l'opération et b) les radiogrammes de l'examen complémentaire.

RÉSUMÉ

Il s'agit d'un examen complémentaire de 41 cas de forage du col fémoral chez 39 patients. Juste après l'opération, il y avait une amélioration chez env. 90 %, 6 mois après le chiffre des améliorations était env. 76 %, deux ans après env. 70 %, et 6 ans après env. 64 %. La durée des symptômes et la motilité avant l'opération ainsi que l'étiologie semblent être sans aucune importance pour l'indication; par contre on pense pouvoir constater, sur la base de l'examen radiologique avant l'opération, que les grands kystes et une raréfaction osseuse prononcée ainsi qu'une faible éburnation sont pronostiquement un bon signe par opposition aux kystes entourés d'un tissu éburnisé et seulement avec une raréfaction osseuse minime. Simultanément avec la disparition des douleurs, les kystes se diminuent et la raréfaction osseuse est remplacée par un tissu éburnisé.

SUMMARY

41 forages of the femoral neck were performed on 39 individuals. Control examinations showed the following. Immediately after the operation there was amelioration in about 90 per cent, at the end of six months in about 76, of two years in about 70 and of 6 years in about 64 per cent of the cases. The duration of the symptoms and the grade of motility before the operation as well as etiology do not seem to be of any significance for the indication. On the basis of roentgenograms taken previous to the operation it may be assumed that large cysts, marked atrophy of the bone and slight eburnation viewed in the light of prognosis are favourable signs, whereas this does not seem to hold good for cysts surrounded by compact bony tissue and if only a slight atrophy of the bone is present. Simultaneously with the regression of the pains the cysts diminish in size and the atrophic section of the bone is replaced by bony tissue.

ZUSAMMENFASSUNG

Es handelt sich um eine Nachuntersuchung von 41 Fällen von Bohrung des Schenkelhalses bei 39 Patienten. Gleich nach der Operation waren etwa 90 % gebessert, 6 Monate später betrug die Zahl der Gebesserten 76 %, 2 Jahre nach der Operation etwa 70 % und 6 Jahre nach derselben etwa 64 %. Die Dauer der Symptome und die Beweglichkeit vor der Operation, wie auch die Ätiologie, scheinen für die Indikationsstellung völlig ohne Bedeutung zu sein. Im Gegenteil — man hat gemeint, an Hand von röntgenologischen Untersuchungen vor der Operation feststellen zu können, dass grosse Zysten und ausgesprochene Knochenatrophie sowie schwache Eburnisation prognostisch günstige Zeichen darstellen, zum Unterschied von Zysten, die von kompakten Knochengewebe umgeben sind, das nur minimale Knochenatrophie aufweist. Gleichzeitig mit dem Verschwinden der Schmerzen werden die Zysten kleiner und der atrophische Knochen wird durch kompaktes Knochengewebe ersetzt.

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FROM THE ROENTGEN CLINIC OF THE STATE HOSPITAL, COPENHAGEN
(CHIEF: PROF. P. FLEMMING MØLLER, M. D.)

THE VALUE OF KYMOGRAPHY FOR THE DIFFERENTIAL DIAGNOSIS BETWEEN ANEURYSM OF THE AORTA AND MEDIASTINAL TUMOR[1]

by

Bryan Fabricius

Though the clinical differentiation of aneurysm of the aorta from mediastinal tumor probably no longer causes much difficulty, the roentgenologic diagnosis between the two conditions is not yet absolutely sure, because they both may be found in precisely the same places in the mediastinum and be of the same homogeneous structure. If the screening shows a soft-tissue shadow intimately connected with the shadow of the vessel, the probability is for the presence of an aneurysm; but the opposite by no means excludes that diagnosis; since it may be a case of SCHATZKI's peduncular aneurysm.

Neither does the heart play any rôle so far as the differential diagnosis is concerned. Thus, it has been found by LAQUEUR & KIMMERLE that the breadth of that organ is not increased in luetic aortitis, and corresponding to this, I have at examination of 10 cases of that affection found increase of the breadth of the heart only in 2 instances. Among 29 cases of aortic aneurysm in patients with hypertension and arteriosclerosis there were 17 in which the breadth of the heart was increased; while among 11 cases of mediastinal tumor I found 2 in which the patient's heart was too large.

Nor yet are calcareous deposits in the aorta a sure sign of aneurysm, inasmuch as RUSBY describes the finding of such in the margin of dermoid cysts in the mediastinum. KIENBOECK gives the rule, named after him, according to which there in luetic aneurysms of considerable size, where the ascending aorta is saccularly or cylindrically distended, on close observation may also be seen a slight, diffuse, fusiform or cylindric dilatation of the adjoining portions of the aorta. If one sees an apparent di-

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latation of the ascending aorta without any noticeable widening of its adjoining parts, it should therefore be an indication of tumor. The opposite, — that is a slight dilatation of the surrounding parts, — must not, however, be taken as proof of the presence of an aneurysm; neither does the rule apply in dissecting aneurysm.

With regard to the movements, FETZER says that an intrathoracic struma moves upwards under deglutition, which according to him should be a sure diagnostic sign. But this is not always the case; for SCHATZKI reports a case, in a woman with strong dyspnea, in whom roentgen examination disclosed a plum-sized spherical tumor between the upper margin of the aortic arch and the trachea, with constriction and displacement towards the right of the latter; which distinctly moved when the patient swallowed or coughed, and which at necropsy was found to be a walnut-sized, spherical, peduncular aneurysm of the beginning of the aortic arch.

According to LENK, pulsation is neither a positive nor a negative sign, so far as the differential diagnosis is concerned; because in the case of large aneurysms with thrombi along the wall the margin is immovable, whereas tumors intimately connected with the aorta may show distinct communicated, and highly vascularised tumors, even active pulsation. Thus, there is no sure sign by which the roentgenologic differentiation between the two conditions may be guided, and in the course of time many cases have, in fact, been reported, in which the roentgenologic verdict has tended one way but necroscopy has proved the other to be the right. It is therefore not surprising that when the kymograph was introduced it was hoped that it would be possible by the aid of this device to solve the problem of the differential diagnosis.

The information obtained by means of the kymograph (which in its present form is constructed by STUMPF), concerns partly the course of the marginal curve, partly the changes in intensity. While the marginal curve of the left ventricle is due very largely to an actual change of volumen, the marginal movements in the aorta are, as shown by WELTZ, chiefly the result of altered position of the whole aorta, whereas the changes in volumen play only a very little rôle. The marginal curve in the ascending aorta is a mixed curve resulting from the combination of the movements in the superior vena cava and the ascending portion of the aorta, the latter of which never, normally, forms a margin here (GROEDEL; DELHERM & CHAPERON). Nor have I in examinations of 150 normal subjects in ages between 17 and 34 years in any case found the aorta forming a margin on the right side. The movements thereby produced are slight and, as a rule, hidden by the spinal column, and are therefore of little interest. For the same reason, no changes in intensity are seen here, either.

In the arch, and in the thoracic portion of the aorta until the latter becomes hidden behind the shadow of the heart, both distinct marginal curves and changes in the intensity are seen. The course of the marginal curve is here very constant; the systole is a straight, horizontal line, until it with a sharp bend continues over into the diastole, the course of which is more oblique, and in which there is seen a small notch corresponding to the end of the systole and the closing of the semilunar valves. If a kymogram is taken with a rapidly dropping grid diaphragm, so that the waves become sharper, it will be found that the systolic leg, at the end of the systole, when the pressure in the ventricle begins to fall, passes over into a convex arc; and not until this has moved a little over towards the middle, and the pressure has become greater in the aorta than in the ventricle, do the semilunar valves close, whereby the notch is produced. The diastole then continues in an even, oblique line, which again abruptly passes over into the systole. The changes in the intensity are seen most distinctly in the left ventricle and the aortic arch, and are due to the shifting blood volume there. During the systole, part of the blood in the ventricle will be forced out into the aorta and its volume diminishes, while its transparency increases until it reaches its maximum at the height of the systole; whereupon the blood volume during the diastole again increases and the transparency decreases until the height of the diastole. Corresponding to this, the varying density in the ventricle will in the kymogram be found to express itself in alternating light and dark horizontal stripes, merging evenly into each other; the lighter ones corresponding to maximum diastole, the darker to maximum systole. This is seen most distinctly with narrow hearts fixed in a straight upward position; in these the rarefactions can at the apex be followed all the way inwards to the spinal column. On the other hand, if the functional capacity of the heart is reduced, so that the amount of residual blood is increased, the difference between the amount of blood it contains during diastole and systole, and therefore also the difference between its transparency during the two phases, will be less, and the rarefactions, in consequence, disappear either partly or altogether.

The same, but in reverse order of sequence, is the case in the arch of the aorta. Here, the rarefactions will be most distinct during maximum systole and faintest during the diastole; on the other hand they are much more constant than in the left ventricle, and in normal hearts I have always been able to demonstrate them.

Several authors have thought that these kymographic features enabled them to distinguish between an aneurysm and a tumor; either, as FISKE, MEYER and SCHOENEBERG, because they believed that in the case of the former there were marginal movements, in the case of the

latter not; or because they, as GUBNER, SCHMIDT & UNGERLEIDER and SCOTT & MOORE, found that in the case of aneurysms the intensity varies corresponding to the cycle, whereas in the case of tumors it is constant; which made them believe that the kymograph was a valuable aid to distinguish between the two conditions. Nevertheless, they are obliged to admit that the differential diagnosis is difficult. MEYER further believes that the movements in aneurysms are synchronous with those of the aorta, while the movements in the tumors lag a little behind.

In the following, I give the results of the kymographic examinations and show to what extent they were of value for the differential diagnosis in 29 cases of patients with aneurysms either of the ascending aorta, the aortic arch or the intrathoracic portion of the descending aorta, and in 11 cases of mediastinal tumor.

In the cases in which the ascending aorta was dilated and therefore formed a margin on the right side, normal vascular waves, and in a few cases also slight rarefactions, were found as signs of this. In the arch and the descending aorta, normal rarefactions, synchronous with the cycle, were found in 21 of the 29 cases. In all the cases there were at the same time distinct vascular waves along the margin, though of lesser amplitude than in normal subjects, in whom the mean for the 150 cases examined by me was 2.8 mm.; whereas the average amplitude for the aneurysms was 2.0 mm., varying from 1 to 3 mm. The form of the waves was in many cases different, the systolic leg running obliquely downwards instead of horizontally; because the lateral movement of the wall is slower, owing to wasting of the elastic fibers of the latter and formation of connective tissue, which makes the wall stiffer and more unyielding. On the same account, the diastole runs more perpendicular than normally; the wall returning more slowly to its original position; and the notch is entirely absent. The following is an example of this group of cases.

State Hospital, Copenhagen, (med. service B); case-no. 892/43. — Woman, aged 52 years; formerly well. Admitted for arterial hypertension and hypertensive encephalopathy. In the last 6 months 3 times fainting-spells of several days' duration, once with paralysis of the right arm. Complains of headache, dizziness, double vision, sudden darkness before the eyes, pricking pains in the heart region and dyspnea.

Objectively, there was no cyanosis or any dyspnea when she was at rest. Stethoscopy of the heart showed it increased in breadth, but there were no abnormal sounds. Stethoscopy of lungs: nothing abnormal. Blood pressure: 240/160. Electrocardiography: nothing abnormal.

Roentgen examination showed a normal heart measuring 13 cm., while the transverse diameter of the thorax was 27 cm.; the vascular trunk diffusely ectatic, measuring (max.) 9.5 cm. — Lungs: clear.

Kymography (Fig. 1) showed, corresponding to the left border of the heart, distinct double waves, due to a pendulum movement of the whole heart during a part of the systole, such as seen, for instance, in hypertension. The ascending aorta showed almost

indistinct double waves, but corresponding to the arch and the descending aorta there were normal vascular waves, 3 mm. wide, with distinct rarefactions.

In the other 8 cases there were no rarefactions; the structure of the whole visible portion of the aorta was entirely uniform. This was partly due to the fact that these aneurysms were the largest, both in the frontal and the sagittal plane, and the part of them to be passed by the roentgen rays therefore so large that the vascular shadow came to stand out homogeneous both during the systole and the diastole; and possibly also, — though no distinct calcareous deposits were seen in the wall, — to more or less considerable thickening of the latter. In 6 of these cases there were waves of the same appearance and amplitude as described above.

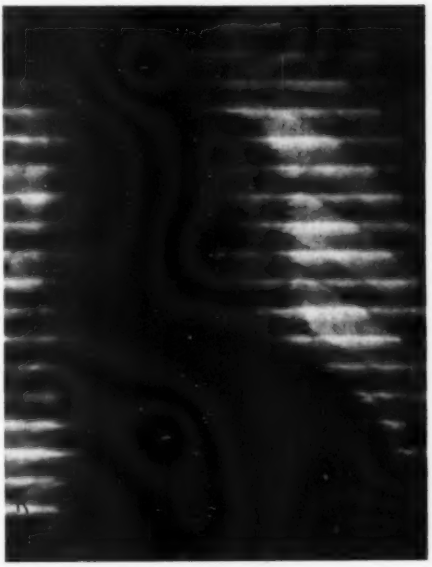

Fig. 1.

In the last two patients with aneurysms there were no marginal movements in the arch or the descending portion of the aorta. One of them was a man, 68 years old, with lues and increasing functional dyspnea, in whom there on stethoscopy was found dullness behind the manubrium of the sternum, and in whom the roentgen examination showed a large, almost completely calcified aneurysm of the aortic arch, corresponding to the branching-off point of the left subclavian artery, and probably extending out into the latter and occupying the entire upper half of the right pulmonary field. In this case, the absence of any marginal movements is readily explained, partly by the size of the aneurysm, which entirely eliminated the difference between the systolic blood pressure and the diastolic, and thereby the cause of the marginal movements; partly the very great calcareous deposits, which made the wall rigid. The other case was as follows:

State Hospital, Copenhagen, (venerol. service), case-no. 938/42. — The patient, a man aged 51 years, had been well until 1938, when he was found to have lues, without known primary infection; whereupon he underwent several cures. Otherwise well; particularly no symptoms referable to the heart. Stethoscopy and electrocardiography, nothing abnormal. Wassermann reaction strongly positive.

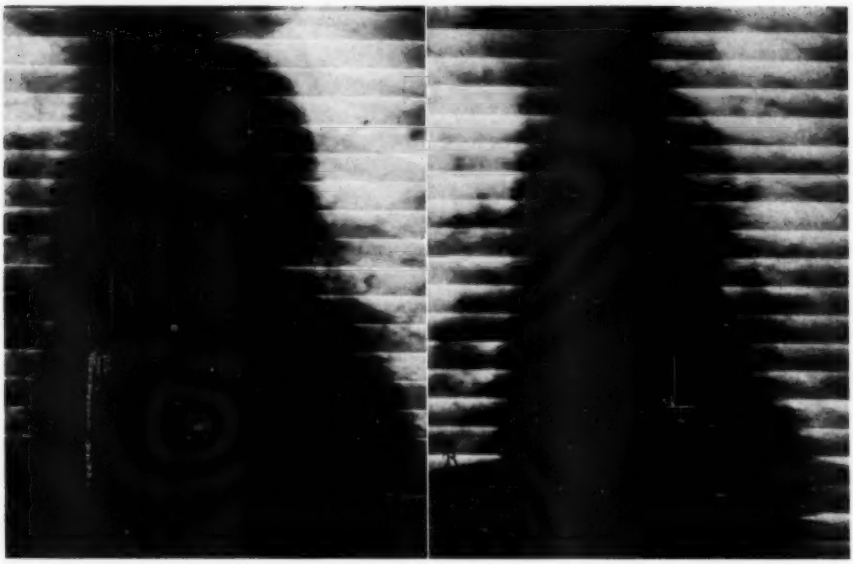

Fig. 2. Fig. 3.

Roentgen examination showed a normal heart measuring 15 cm., while the transverse diameter of the thorax was 31 cm. The vascular trunk was diffusely ectatic, its transverse diameter 10 cm., and there was a distinct calcareous plaque in the arch of the aorta.

The *kymogram* (Fig. 2) showed nothing particular corresponding to the right and left borders of the heart. Corresponding to the ascending portion of the aorta were seen 4 large vascular waves with a distinct notch, but no rarefactions. The margin of the entire arch and descending aorta was completely immobile and without rarefactions.

The following case is given in order to show the influence of the calcareous deposits on the marginal movements:

State Hospital, Copenhagen (med. service A); case-no. 967/43. — Man, aged 68 years, admitted for thyreotoxicosis; but, besides, for a year past suffering from increasing functional dyspnea. Stethoscopy and electrocardiography, nothing abnormal. Wassermann reaction negative.

Roentgen examination showed a normal heart measuring 14 cm., while the transverse diameter of the thorax was 29 cm. The arch and descending portion of the aorta were dilated. The vascular trunk measured, in all, 9.8 cm., and there were distinct calcareous deposits in the arch.

The *kymogram* (Fig. 3) showed nothing abnormal corresponding to the right and left borders of the heart. The ascending aorta was hidden by the spinal column, but corresponding to the arch and the descending portion there were, despite the calcareous deposits, perfectly normal rarefactions and vascular waves, 3 mm. wide, with oblique systolic and almost perpendicular diastolic legs.

The absence of marginal movements in case 2 can therefore not have been due to the calcareous deposits, even if these perhaps have played a certain rôle. Nor yet was the aorta so ectatic that it can have been the cause, and it must therefore be considered if there should not be thrombi along the wall, which might account for the immobility of the margin.

Of the 11 cases of mediastinal tumor, 6 were lymphogranulomatoses. In the roentgenograms of the thorax they all showed increased breadth of the mediastinum shadow, which diminished considerably after roentgenologic treatment. In one case there was a deeply situated intrathoracic struma, verified by operation; one case was due to lymph node metastases from a very small cancer in the lung, situated anteriorly in the mediastinum, arisen from the hilus and verified by necropsy; one case was due to lymph node metastases from an esophagus cancer, situated between the esophagus and the trachea and in the anterior view showing as a roundish soft-tissue shadow to the right of the mediastinum shadow and connected with the latter.

The following case is given as an example of the kymographic picture in mediastinal tumors.

State Hospital (surg. policlinic); case-no. 686/44. — Man, aged 37 years, who in 1937 had had his right testis removed on account of tuberculosis, but who had since been well until 3 weeks before he came to the policlinic because his left testis began to get swollen and tender to the touch. No fatigue or loss of weight; no sensation of fever; no symptoms from the urinary tract.

Objectively, right testis absent, left testis fully hen's egg-sized, tender, without redness of warmth. The epididymis situated upwards, firm, not tender to touch. Microscopy of the urine showed hematuria, and cultivation from the latter gave growth of tubercle bacilli. Urography showed poor filling of the upper renal calyces in both sides, wherefore the patient was admitted to the surgical ward for more thorough examination. — Stethoscopy, nothing abnormal.

Roentgen examination of the thorax showed very considerable increase in breadth, to both sides, of the central shadow, in the side views seen to be due to large lymph node shadows arising from the hilus and probably due to tuberculosis, since also tuberculous infiltration was found in the region of the apex.

Kymography (Fig. 4) showed nothing abnormal corresponding to the heart itself, but the soft-tissue shadow showed uniform intensity and complete immobility of the border, while centrally in the latter there could faintly be discerned a normal aorta with normal vascular waves.

Finally, the following case is given, because it showed a kymographic picture different from all the foregoing ones.

State Hospital (med. service A); case-no. 435/39. — Man, aged 20 years, formerly well. His present affection had begun 2 months previously, with cold, cough and stitch in the right side. With rest in bed for a week the condition had improved, but when he afterwards got vaccinated against cold the pain in the chest returned, wherefore he was admitted to the hospital in his town. During his stay there, his temperature rose to max.

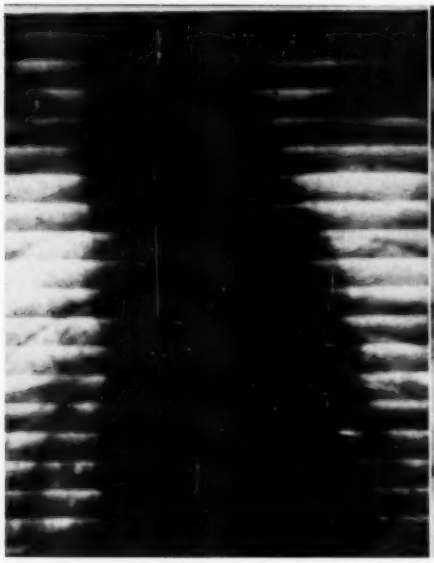

Fig. 4.

Fig. 5.

38.7° C., but otherwise he was well and had no pain in the chest. A tumor was found, however, in the mediastinum, and he was therefore transferred to the State Hospital. No cardiac symptoms.

Objectively, no cyanosis or dyspnea. No peripheral adenitis. Stethoscopy of the heart: nothing abnormal. Stethoscopy of the lungs: no murmurs, but to the right of the sternum percussion detected a tumor, which merged into the cardiac dullness. Blood pressure, 135/60. Wassermann reaction negative.

Roentgen examination of the thorax showed, issuing from the central shadow, a large, rather sharply circumscribed soft-tissue shadow, of slightly wavy outline, extending into the thoracic cavity. In the frontal view it lay outside the hilus area, in the lateral view quite anteriorly in the thorax, in front of the trachea, and seemed to extend all the way to the anterior wall of the thorax. The heart was small, and no dilatation was seen of the arch or the descending aorta.

The *kymogram* (Fig. 5) showed nothing of interest corresponding to the right and left heart borders. In the arch and the ascending aorta were seen large, normal vascular waves, 4 mm. wide, with notch and distinct rarefactions; and about 1 cm. to the right side of the spinal column the descending aorta could be just barely discerned as a continuation of the right heart border, with feeble vascular waves shining through the soft-tissue shadow. The border of the latter showed waves, 3 mm. wide, the lateral movements of which began synchronously with the lateral movement of the aorta, with a horizontal, lateral course, which, rounding off, continued over into the medial movement. The latter began simultaneously with the medial movement of the aorta, but its course was almost horizontal, so that it reached its medial position early in the diastole, whereupon it during the last part of the latter ran perpendicularly, before it again took a

lateral course. Corresponding to these waves there were distinct rarefactions, which could be followed for as much as 3 cm. into the shadow.

The patient was given a trial irradiation, of 1,500 r in all, to two fields on the supposed tumor; but the latter did not change and must therefore be assumed to have been a congenital, benign growth. The movements along its border have been described; but the distinct rarefactions, which were due to changes in volume, give grounds for suspecting that there, besides the communicated pulsations, have been pulsations in the tumor itself, and that it must thus have been highly vascularised.

At the time of his discharge, the patient was completely well. He was admitted, for control, 3 months later, was at that time still symptom-free, able to attend to his work, and had put on weight. The tumor in the thorax was quite unchanged.

It will thus be seen that though there in kymograms of aneurysms most often are both rarefactions and waves corresponding to these, so that the diagnosis in these cases is not difficult, there are also cases in which one or the other of these features is lacking, so that there is only seen a uniform, homogeneous, immobile shadow. On the other hand, there are, though rarely, cases of tumor in the mediastinum in which both rarefactions and distinct marginal movements occur; and the conclusions must therefore be that the kymogram alone, as little as ordinary roentgenograms or screening, enables one to establish an exact diagnosis.

SUMMARY

As the result of kymographic examination of 29 cases of aortic aneurysm and 11 cases of mediastinal tumor, the author shows that kymography, as little as any of the other roentgenologic examinations separately enables one to distinguish with certainty between the two diseases; because there is not always in the former found either linear rarefactions or marginal movements corresponding to the changing blood volume; while, on the other hand, both these phenomena may sometimes be found in the latter, when the tumor is highly vascularised or intimately connected with the aorta.

ZUSAMMENFASSUNG

Als Ergebnis der kymographischen Untersuchung von 29 Fällen von Aortaaneurysma und 11 Fällen von Mediastinaltumor weist Verf. nach, dass die Kymographie, ebenso wenig wie irgend eine andere röntgenologische Untersuchung allein, die Möglichkeit gibt, diese beiden Krankheiten mit Sicherheit zu unterscheiden. Bei ersterer Krankheit kommen nämlich weder lineare Aufhellungen noch mit dem wechselnden Blutinhalt übereinstimmende Randbewegungen immer vor, während diese Symptome manchmal beide bei der letzteren Krankheit gefunden werden, wenn nämlich der Tumor stark gefässführend ist oder sich eng an die Aorta anschliesst.

RÉSUMÉ

Après s'être servi de l'examen kymographique dans 29 cas d'anévrisme de l'aorte et 11 cas de tumeurs médiastinales, l'auteur démontre que pas plus la kymographie que n'importe quelle autre méthode radiologique isolée ne permet le diagnostic différentiel

certain de ces deux affections. Dans la première d'entre elles on ne constate pas toujours des éclaircissements linéaires ni des ondes marginales correspondant aux modifications du volume sanguin, alors que ces modifications de l'image se manifestent parfois dans le second groupe, lorsque la tumeur est riche en vaisseaux ou qu'elle est en contact intime avec l'aorte.

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FROM THE RADIUM CENTER, COPENHAGEN (CHIEF: JENS NIELSEN, M. D.)

DOSIS MEASUREMENTS IN ROENTGEN IRRADIATION OF THE FEMALE PELVIS[1]

A Preliminary Communication

by

Anton Jensen

In his work »Cancer, its Diagnosis and Treatment», CUTLER says that »the radiation treatment of carcinoma of the cervix has become the most optimistic and successful chapter in radiation therapy of cancer». Nevertheless there are still many unsolved problems, and the results are far from satisfactory. In Denmark, with its population of about 4 million, there are 550 fresh cases of uterine cancer yearly, and 385 deaths from that disease. The 5-year survival rate with freedom from symptoms is only 30 per cent. In England, the mortality from cancer of the uterus was, in 1935, 134 per million of female inhabitants; with a population of 38.5 million, half of which are women, this gives a total of 2,580.

The poor results are no doubt due, in a measure, to the fact that the patients do not present themselves for treatment until the disease has reached an advanced stage, where the prospect of complete cure is slight; but even with complete and correct treatment in the early stages there are still many recurrences. Thus, HEYMAN gives, in 1935, the results of radiation treatment of cervical cancer at the Radiumhemmet in Stockholm during the period 1914—1928 as follows. The total number of examined cases was 1,537. Of these, 327 (= 21.3 per cent) were symptom-free after 5 years. Of cases in Stage I, 141 were treated and 81 of them (= 58 per cent) cured; of cases in Stage II, 403 were treated and 138 of them (= 34 per cent) cured. In 1941, BERVEN gives the figures for Stage I and II as respectively 67 and 39 per cent.

[1] The work was carried out with support from the Danish National Anti-Cancer League. Submitted for publication, Sept. 26, 1944.

If there shall be any hope of bettering the results, the pathologic anatomy of the disease and the clinical features of the recurrences must be studied. It is well known that distant metastases are comparatively rare; according to EWING 16 per cent.

As a rule, the disease spreads either in continuous manner or along the lymph channels out into the parametria, and gradually all the way out on the wall of the pelvis. There are lymph glands both along the vessels of the parametria and on the pelvic wall, especially on the anterior aspect of the sacroiliac joint, below the bifurcation of the common iliac artery (KUNDRAT; KERMAUNER & LAMARIS; SCHAUTA). Also the urinary bladder and the rectum may become involved, but the most frequent cause of death is uremia due to compression of the ureters (EWING; DREXLER & HOWES).

For radiation treatment of cancer of the uterine cervix, most authors prefer radium. This is especially the case as regards the Stockholm method, which is the one most used in the Scandinavian countries, and to some extent in England (HEYMAN, CHIEWITZ, CHYDENIUS, HURDON). In France and Belgium, the so-called Paris method, from the Curie Institute, is the one most used (REGAUD, LACASSAGNE, MATHEY-CORNAT). It works with lesser quantities of radium and longer exposure time, in recent years also with large doses of roentgen to the parametria. In Germany, roentgen treatment has been more in favor (VOLTZ, REICHENMILLER, WINTZ).

At the radium Center in Copenhagen, intracavitary radium treatment was until 1937 the only method used, and then nearly always after a modified Stockholm method, with 2 treatments, each of about 3,300 mg. hours. In the upper end of the vagina were placed 2 cylindric leaden tubes, with walls 3 mm. thick, each containing 50 mg. of radium element, and in the uterus a platinum tube, 5 cm. long, its wall 0.5 mm. thick, containing 70 mc. of radium emanation. Treatment time, 20 hours, in uncomplicated cases 10 days' interval between the two treatments; total dose about 6,600 mg. hours. For further details I refer the reader to a paper by FR. TRUELSEN (not yet published).

It was thought, however, that the results might be improved by giving a supplementary roentgen treatment, such as is now given in most places in other countries; but the lack of sufficient beds for the many patients made this impossible. The radium treatment may give a strong cancericidal dose on the tumor itself, but out on the pelvic wall, where most of the lymph nodes are situated, the ordinary radium treatment gives only 1,000 to 2,000 r, because the dose diminishes with the square of the distance (FRIEDRICH; KIRCHHOFF & BEATO; WASSERBURGER & SMEREKER; MAYNEORD & HONEYBOURNE, and others).

In collaboration with Mr. BORGE MADSEN, M. Sc., I have, by means of the usual formulae (SIEVERT, ZIMMER, MINDER), worked out isodose curves for the most frequent combination with 2 lead tubes transversely in front of the portio and a platinum tube in the uterus (Fig. 1). It will be seen that the intensity at a distance of 5 cm., corresponding to the pelvic wall, is only 50 r/h., which in 2 × 20 hours gives 2,000 r. The dose may be noticeably increased by placing the tubes far out to the sides, in the same way as REGAUD's colpostat, but the increase obtained is far from sufficient. These problems will be discussed in greater detail in a later paper.

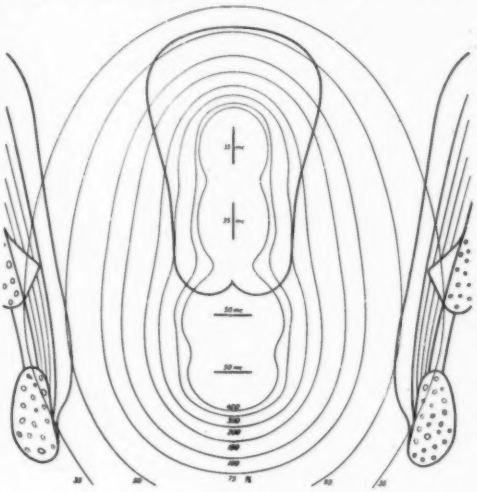

Fig. 1.

In the summer of 1937, the new premises of the Radium Center were ready for use, with 104 beds, and it now became possible to introduce the combined radium- and roentgen treatment. In the beginning, 4 fields, of 10 × 10 and 10 × 15 cm., were used (JUUL); later, 8 fields, of 10×10, 12.5×12.5, and 10×15 cm. became the rule (JENS NIELSEN). In order to determine the intensity and the distribution of the dose in depth, it was decided to make a series of measurements on an anatomic preparation of a female pelvis, partly with the fields used, partly with large fields after the method of WARNEKROS & DESSAUER.

Dosis Measurements on Anatomic Preparation

The female pelvis used measured 30 cm. in height, from 5 cm. above the umbilicus to 5 cm. below the vulva. The circumference at the height of the upper border of the symphysis, which corresponds to the location of the cervix, was 96 cm.; the antero-posterior diameter 23 cm., the transverse diameter 32 cm., the weight 19.3 kg. The preparation was sawn through in the midline, and the right half dissected out, so that the uterus and the vessels of the pelvic wall lay exposed. For the purposes of the measuring, the right side was filled with bags of talcum, and the preparation gathered in a canvas corset and wrapped in a sheet; because the irradiation had to be done on the usual treatment couch for the

patients. As measuring apparatus was used a Siemens universal dosimeter, the thimble chamber of which was set into the place where the measuring was to be done, through a cardboard tube. As in the treatment of the patients, the factors worked with were 180 kv., 6 ma., focus-skin distance 50 cm.; and filter 0.5 Cu., which corresponds to a half layer value of 0.9 Cu. The intensity, measured in air with Kuestner's dosimeter, was 18.8 r/min., or 100 r in 5.3 minutes.

The intensity was measured in the following 6 places: (1) the middle of the cervix; (2) the middle of the vagina; (3) the right pelvic wall, 5 cm. laterally to the cervix; (4) the right pelvic angle, about 7 cm. upwards and laterally to the cervix; (5) the urinary bladder, about 3 cm. in front of the cervix; (6) the rectum, about 3 cm. back of the cervix. The pelvic angle is the portion in front of, or below the sacroiliac joint, just below the bifurcation of the common iliac artery. Here most of the lymph glands are situated.

A great many different fields, both large and small, were measured, but for the sake of ready survey only the principal combinations are given here:

I. — *2 large fields*, 20 × 24 cm., an anterior and a posterior, both at the level of the symphysis, centered on the cervix.

II. — *4 large fields*, 20 × 24 cm. Besides the two formerly mentioned, 2 lateral fields at the same level.

III. — *4 medium-sized fields* (JUUL): one, 10 × 15 cm. transversely over the symphysis; one 10 × 15 cm., obliquely from below on the coccyx; and two natis fields, each 10 × 10 cm., about 45° obliquely in from the side and back, over the sciatic foramen (BACLESSE); all sighting toward the middle of the pelvis.

IV. — *8 medium-sized fields* (JENS NIELSEN): 2 anterior, 12.5 × 12.5 cm., corresponding to the iliac fossa; 2 lateral, 10 × 15 cm.; and 4 posterior, the two upper 10 × 15 cm., the two over the nates 12.5 × 12.5 cm. Also here, all the fields centered on the cervix (Fig. 2).

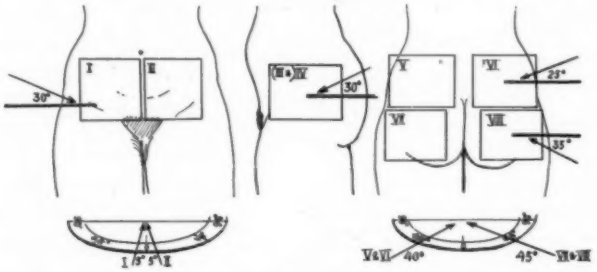

Fig. 2.

The results are shown in Table I. »I» is the intensity, measured in r/min.; it is the sum of the measured intensity for all the fields. Next, is stated the intensity in per cent of the intensity on the cervix. By JUUL's treatment (JUUL) is understood the aggregate depth dose in r with 100 r × 24, measured in air, on each of the fields. By JENS NIELSEN's treatment is understood, correspondingly, the aggregate depth dose with the technic now used, with 200 r × 10 on each of the anterior fields, 200 r × 6 on the lateral 200 r × 7 on the posterior fields, likewise measured in air.

JUUL gave 100 r daily to all 4 fields, which usually resulted in a dry epidermitis and moderate rectal reaction. JENS NIELSEN now gives 200 r daily, to 2 fields.

Table 1

		2 large fields	4 large fields	4 medium-sized fields	8 medium-sized fields
On the Cervix	I r/min	20.7	29.0	21.2	34.5
	Per Cent	100	100	100	100
	JUUL	2,633	3,689	2,698	4,025
	JENS NIELSEN				2,810
In the Vagina	I r/min	21.9	31.1	19.2	25.6
	Per Cent	106	107	91	74
	JUUL	2,787	3,957	2,444	3,257
	JENS NIELSEN				2,123
On the right wall of the Pelvis	I r/min	20.0	29.8	20.3	31.3
	Per Cent	97	103	96	91
	JUUL	2,544	3,791	2,584	3,982
	JENS NIELSEN				2,427
Below right pelvic angle	I r/min	18,5	27,2	19,0	29,8
	Per Cent	89	94	90	86
	JUUL	2,354	3,461	2,419	3,792
	JENS NIELSEN				2,391
In the urinary bladder	I r/min	20.4	31.0	18.7	30.6
	Per Cent	99	107	88	89
	JUUL	2,595	3,943	2,380	3,893
	JENS NIELSEN				2,519
In the Rectum	I r/min	21,0	31.4	23.7	39.4
	Per Cent	101	108	112	114
	JUUL	2,671	3,995	3,017	5,013
	JENS NIELSEN				3,080
Size of Fields cm²		960	1,920	500	1,225
Variation in the Distribution (Per Cent)		+ 6 17 ± 11	+ 8 14 ± 6	+ 12 24 ± 12	+ 14 40 ± 26

The measurements show that about the same depth dose can be obtained with 2 large fields as with 4 or 8 fields of the usual size. It is

thus a very speedy and economic method, which at the same time gives a good distribution in the depth, with only 17 per cent variation. The cervix, the urinary bladder, the rectum and the wall of the pelvis all get nearly the same dose, the vagina gets too much and the pelvic angle too little. But this could in practice easily be equalized by moving the fields a few centimeters higher up.

With additional irradiation to 2 lateral fields, a still better distribution is obtained, with a variation of only 14 per cent. Of course, the dose will then be increased by 50 per cent; but at the same time both the irradiated area and the treatment time is doubled. The 4 medium-sized fields give a good dose in proportion to the area irradiated, which is only 500 sq. centimeters; but on the other hand the distribution gets more uneven. With the 8 medium-sized fields now used, a still larger depth dose is obtained, but at the same time the distribution also becomes more uneven. That the dose in the vagina is low, is no doubt immaterial. If that organ is very much involved, a supplementary field on the vulva may be irradiated. Of greater importance are undoubtedly the doses to the wall of the pelvis, and below the pelvic angle, which corresponds to the lateral part of the parametria and the large vessels, where the lymph glands are situated. By the intracavitary radium treatment with 7,000 mg. hours, these more distant parts get only between 1,000 and 2,000 r, whereas the cervix and its immediate surroundings get between 6,000 and 8,000 r, in other words a surely cancericidal dose.

In practice, it is, as a rule, not the skin dose, or the cutaneous reaction, but the reaction in the rectum, that is determining for how far one may risk to go with the total dose (LACASSAGNE, TODD, MUDD). It is therefore of great importance to see how great intensity is obtained there with the different methods. If we take the rectal dose as basis for the estimate, it will below the pelvic angle be, with 2 large fields 88 per cent, with 4 medium-sized fields 78 per cent.

We have not attempted, as done by WACHSMANN and CHAOUL, to calculate the volume dose; but it is evident that it is on account of the latter that large fields are used so little. For the sake of comparison, the irradiated areas are stated. All else being equal, they give at least an expression for the volumes irradiated, and thus also for the volume doses.

Dosis Measurements on Patients with Cancer of the Uterine Cervix

Also on patients with cervical cancer a number of measurements were done, the dosimeter chamber being introduced into the vagina, up against the uterus. Thus, here only the dose on the cervix could be measured. The results are shown in Table II.

Table II

No. of Patients	Weight	Anterior Field	Upper Natis Field	Lower Natis Field	Lateral Field	Total
7	under 60 kg.	7.9 r/min.	4.5 r/min.	7.0 r/min.	2.5 r/min.	43.9 r/min.
20	over »	6.5 »	5.1 »	6.8 »	1.8 »	40.5 »
Mean	69 kg.	6.6 r/min.	5.0 r/min.	6.9 r/min.	2.1 r/min.	41.1 r/min.

Intensity in the vagina, at the cervix, for different fields used in the 8-field technic (NIELSEN) measured on patients.

With the usual technic of 200 r × 10 to the anterior fields, 200 r × 7 to the posterior, and 200 r × 6 to the lateral, the values in a complete series were, from the anterior fields, 1,400 r; from the upper natis fields, 742 r; from the lower natis fields, 1,024 r; from the lateral fields, 267 r; total from all fields, 3,433 r. This is somewhat more than found on the anatomic preparation, which only gave 2,810 r on the cervix; but it must be remembered that on the patients it is possible to compress; what cannot be done on the preparation. Also the adjustment is no doubt easier in the case of patients, where one can both see and feel the anatomic points.

Rotatory Irradiation of the Pelvis

So far as it can be seen, rotatory irradiation was first attempted by POHL, in Kiel, in 1906, and described by HANS MEYER, in 1913, in the Zentralblatt f. Gynaekologie; but only in recent years has the therapy been taken up to a more considerable extent. To DU MESNIL DE ROCHEMONT, especially, belongs the merit of having established the general laws for the dose distribution, on the basis of a long series of minute measurements and calculations. Gradually, the therapy has been taken up in several places; in Germany by BENDER & KOHLER, DESSAUER, GUENSEL, HENSCHKE, MAYER, RAHM, and others, in Japan by NAKAIDZUMI and MIYAKAWA, in France by MALLET & PROUT, in the U. S. A. by FLAX and HAWLEY. In Denmark, it was introduced in 1941, by JENS NIELSEN, at the Radium Center in Copenhagen; and there a long series of dosis measurements have since been made, both on phantoms, anatomic preparations and on patients (JENS NIELSEN, HOEFFER JENSEN, THAYSSEN, WISSENBERG); and at the same time the treatment has been used with good results in about 200 cases of cancer of the esophagus.

It can hardly be supposed, however, that the rotation therapy is generally known among practising radiologists; I shall therefore cite a few particulars from papers of a couple of the authors named above.

JENS NIELSEN writes in the »Nordisk Medicin»: »As rotatory irradiation may be compared to the use of many small fields, each of which is in succession irradiated with a fraction of the full dose, it is immediately evident that the charge on the skin will be very low, whereas the centering of all these small fields in the tumor must result in a very large dose in the latter, . . . and that the smaller the field, the larger will the tumor dose be in proportion to the skin dose.» And in a paper in »Radiology», NATHAN FLAX writes about as follows: »For irradiation of cervical and other centrally situated tumors, the rotation therapy has considerable advantages, because the smallest possible fields are used and the tube is in constant motion. The small fields and the moving tube give an unusually high dose in the depth with low skin dose and exact adjustment, the beam being centered on the middle of the pelvis. While it is unnecessary to dwell on the value of a high depth dose, the importance of exact adjustment must be spoken of a little more fully, as it is a condition for a homogeneous transirradiation of the entire pelvis.

Exact angles for the passage of the beams through the pelvis are the basis for the schematic *technic of multiple fields;* the beams being arranged in such a manner that the greatest possible effect of the crossfire is obtained in the region of the tumor. The least deviation from the stated angle may cause an undesirable disturbance of the distribution of the intensity in the pelvis, to the damage of the normal tissue at the expense of the tumor. It is absolutely necessary that the operator is able to reproduce the scheme by sighting against the invisible, deep-seated tumor according to the stated angle for the beam. With the small fields demanded by the 4, 6 or 7 field technic, the most absolute precision is necessary in the statement of the direction, because an error of a few degrees in the inclination of the tube may result in the beam entirely missing a small, deep-seated tumor, or, if the tumor is sufficiently large, striking only its edge, while the rest of it irradiates to no purpose, and perhaps injures, the normal tissue. The *two-field technic*, which uses only two large fields, an anterior and a posterior, does not require exact angles for the adjustment of the tube, and the distribution in the pelvis corresponds to the schematic values. Unfortunately the deep dose is relatively small. One has the impression that with the multiple-field technic and the wandering tube to be described here, the advantages that can be obtained by the multiple-field technic have been successfully combined with the same exact and homogeneous distribution which can be obtained by the 2-field technic.» Also CHAOUL states that the volume dose with rotatory irradiation is small.

As the rotatory treatment of cancer of the esophagus seemed to give good results, an apparatus was built at the Radium Center also

for the treatment of patients in reclining position, especially patients with cervical cancer (Fig. 3). Until now, about 100 have been treated, most of them individuals thin and of slender build. The distance from the tube to the axis of revolution is 45 cm., the axial field 8×10 cm. The beam is centered on the midline, just above the symphysis, corresponding to the cervix. On patients with an antero-posterior diameter of 20 cm., the size of the anterior and posterior cutaneous fields in the midline is 6.2×7.8 cm., the distance to the tube being 35 cm. With a circumference of 90 cm., the irradiated area is 700 cm^2.

Fig. 3.

On a few patients, the skin- and depth doses were measured, by means of Sievert's chambers, on the skin anteriorly in the midline and in the upper end of the vagina. With the technic used, and with irradiation for 11 min. 24 sec. at a distance of 35 cm., — which corresponds to 400 r measured in air, — the dose was found to be 101 r on the skin and 85 r on the cervix. As a similar belt must be reckoned with on the other side, respectively ventral or dorsal, the total depth dose will be 170 r, or 168 per cent of the maximum skin dose.

Measurements on Phantom of the Pelvis

Most of the measurements were done on a phantom of the pelvis, made of paraffin, to which had been added a suitable quantity of Antimol (Dichlorbenzol, $C_6H_6Cl_2$), so that the specific gravity was 1.0 (O. M. Henriques). The size was about the same as that of the anatomic preparation: length (or height) 25 cm.; length of bone, 5 cm.; circumference at height of symphysis, 98 cm.; antero-posterior diameter, 24.5 cm.; transverse diameter, 36 cm. (Fig. 4).

In the plane surface were bored two rows of holes, down to a horizontal level at the height of the symphysis; one, of 5 holes, from front backwards, along the short axis of the elliptic cut surface; the other, of 7 holes, transversally, corresponding to the long axis. The holes intersected in the center, so that there were 11 in all (Fig. 5). Their diameter was 1 cm., the distance between them 3 cm. When the measuring was to be done, small, cylindric Sievert's condenser chambers, size 0.5 × 2 cm., were placed in long cylindric tubes of vinidur (a mixed polymerisation-product of polyvinylchloride; HENRIQUES), which were inserted in the holes. The irradiation was done, just as in the treatment of patients, with a distance from focus to center of 45 cm. and rotation over an arc of 180°. With the milamperage now worked with (15 ma.), a treatment, — ventral or dorsal belt, — can be given in 4.5 min. Axial field, 8 × 10 cm.

Fig. 4.

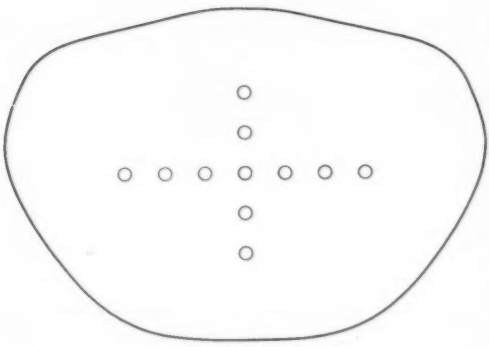

Fig. 5.

Besides the condenser chambers in the holes, one or two chambers were usually placed on the surface, in the midline, and sometimes also corresponding ones on the posterior side, in order to measure the skin dose and the traversing dose. The rotation time, which was controlled with stop-watch, was from 4 min. 12 to 4 min. 41 seconds. Table III shows the distribution along the short axis, in antero-posterior direction.

For the sake of readier survey, the results of a complete revolution of 360°, which consists of a ventral and a dorsal belt, each of 180°, are set down in a scheme corresponding to the location of the holes in the phantom (Fig. 6).

It will be seen that the dose in the center is about the same as the maximum skin dose anteriorly and posteriorly in the midline, but that

Table III

	Ventral Belt		Dorsal Belt	
Skin dose .....××...00.....	90 r.	100 per cent.	9 r.	11 per cent.
At depth of 6 cm.....	80 »	90 » »	17 »	21 » »
» » » 9 »	67 »	75 » »	24 »	29 » »
Dose in center	47 »	52 » »	42 »	51 » »
At depth of 15 cm.	30 »	33 » »	56 »	68 » »
» » » 18 »	14 »	16 » »	70 »	84 » »
On posterior aspect	6 »	6 » »	83 »	100 » »

to both sides there is a considerable diminution, and 6 cm. from the midline, corresponding to the pelvic wall, only 65 per cent of the skin dose, or 68 per cent of the dose in the center.

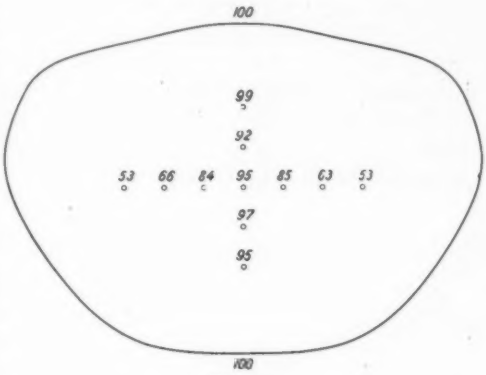

Fig. 6.

The distribution on the surface of the skin was determined by placing the condenser chambers on the latter, with the same distance, about 5 cm., between them, one anteriorly, in the midline, one to each side of this, and the others distributed over the rest of the field. The distribution found was:

Left 45 64 68 75 82 81 84 80 75 67 65 *Right*

The above figures are the number of roentgen measured on a ventral belt of 180°, irradiated in the usual manner for 4.5 minutes. The distribution is not quite symmetric. This is no doubt due partly to error in measuring, partly to a slightly oblique position of the phantom, which had a tendency to sink down in the left side. The outside figures are the doses at the two sides; but the left side was not irradiated for the full time; which was undoubtedly the case with the right, since the dose is of almost the same value as the one next to it.

Double or Oblique Rotation

Rotatory irradiation in one plan gives a relatively small depth dose; namely 103 per cent of the maximal skin dose, if the traversing dose is not reckoned with. I therefore did a series of measurements with the tube adjusted obliquely, alternately from below and above, so that 4

»fields», or belts, were obtained: a vulvar and an abdominal anteriorly, an anal and a lumbar posteriorly; which together formed two rings, or belts, about the phantom. With the usual distance of 45 cm., the width of the belt on the skin was calculated to be 7.3 cm.; the middle of the two belts therefore had to be about 8 cm. apart in order to avoid overlapping. To this corresponded an 18° inclination of the tube.

With such an oblique adjustment, the transirradiated thickness of tissue is increased from 12 cm. to 13 cm. in the midline, while the distribution must remain more or less the same. Perhaps the anterior and posterior portions corresponding respectively to the urinary bladder and the rectum will get a little more, since the belts there overlap at a lesser depth than at the sides. Control measurements with alternately simple and double rotation gave (leaving the traversing dose out of account) in the center: for simple rotation 111 per cent, for double rotation 205 per cent, of the maximal skin dose. With the double rotation it will thus be possible to obtain a sufficient depth dose, even in the case of stout patients.

Rotation at Varying Speed

Among the possibilities which one might think of trying in order to obtain a better distribution of the depth dose, variations in the speed of the tube's rotation during the irradiation is the one which first suggests itself. As the dose is largest anteriorly and posteriorly, because the transirradiated layer of tissue is thinner, it must be possible to reduce the dosage there, — or increase it at the sides, — by increasing the speed of the rotation in the middle sector. I therefore determined the time of rotation with the tachymeter set to different speeds. With the usual adjustment, 850, the rotation over an arc of 180° takes $4^1/_2$ minutes, with adjustment to 650 6 minutes and 18 seconds. The 180° rotation was now divided into 3 equal parts of 60° each:

1) right side, run at low speed, 650, for 2 minutes;
2) middle sector, run at greater speed, 850, for $1^1/_2$ minute;
3) left sides, again run at low speed, 650, for about 2 minutes.

The total rotation time was controlled with stop watch, and besides, the automatic filter control stops the rotation at 180°. The time was found to be close to the calculated $5^1/_2$ minutes.

The distribution of the dose of the skin was:

Left	66	88	92	99	100	87	86	98	93	92	78 *Right*

The values given are the number of roentgens measured, for a usual ventral belt of 180°, with a total rotation time of $5^1/_2$ minutes. As the

highest dose is precisely 100, we have at the same time the distribution expressed in per cent of the maximal skin dose.

The determination of the depth dose was made on the basis of 2 rotations, first from right to left, then from left to right. This gave larger figures and a smaller percentage of error. The values obtained were: along the short axis, in antero-posterior direction

159 203 208 210 192 195 152 r,

along the long axis, to the sides:

167 174 196 210 196 160 143 r.

The first figure and the last, in the first row, are the skin doses on front and back; the first and last in the second row correspond to the dose at a distance of 9 cm. from the center.

From the distribution of the dose on the skin, the maximal skin dose can be calculated, which in the foregoing was used as basis for the distribution per cent in the depth. It was calculated to be 181 r. If we take it to be = 100, we get the following distribution in the depth (Fig. 7).

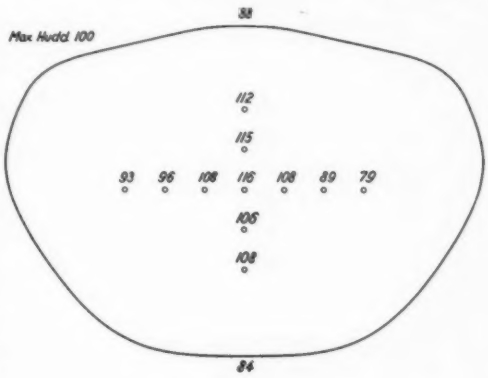

Fig. 7.

As it will be seen from the figures in the scheme, the distribution along the short axis, from front to back, is about the same as in simple rotation, with the exception that there now is a noticeable increase from the skin inwards toward the center. Toward the sides, the distribution is still better; for though there is a diminution, it is not as great as in simple rotation. At a distance of 6 cm. from the center, corresponding to the pelvic wall, there is, with varying speed, 93 per cent of the maximal skin dose, or 80 per cent of the dose in the center; whereas the simple rotation only gives respectively 65 and 68 per cent.

Eccentric Rotatory Irradiation of the Two Sides

As the distribution of the intensity in the depth still was unsatisfactory, irradiation of each side (parametrium) with eccentric rotation was tried, with a smaller field. For the time being, an axial field of

5 × 10 cm. was chosen, which was displaced 3 cm. to the side, so that the two cores just were clear of each other in the midline. The rotation time for 180° was taken a few times with stop-watch, and was found to be 4 min. 33 sec. Half of this, 2 min. 16 sec., thus corresponds to 90°; that is, to the length of the arc described by the tube from horizontal position to perpendicular position over the phantom (Fig. 8). The

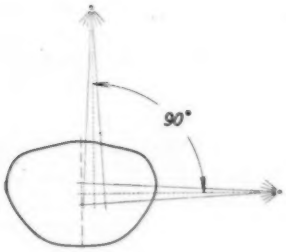

Fig. 8.

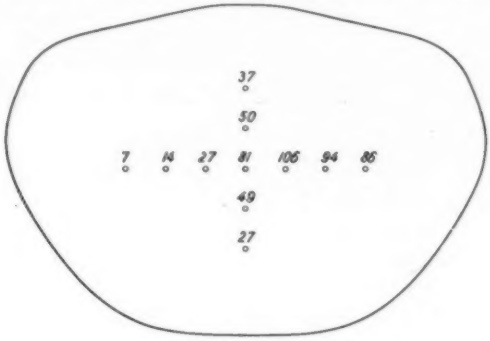

Fig. 9.

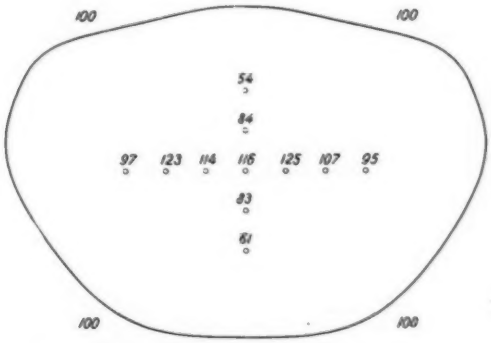

Fig. 10.

depth dose was measured in the usual way, in the already existing holes. The dose on the skin was measured 10 cm. from the midline, because it was not felt certain that full exposure would be obtained at 5 cm.

As in the foregoing experiment, a double irradiation was given, in order to get a larger total dose and the least possible error of measurement. As example of such a treatment is shown here a ventral belt on the right side. Treatment time, 9 min. 06 sec. Skin dose 10 cm. from the midline, 200 r (Fig. 9).

Next, the relative depth dose, expressed in per cent of the skin dose on the respective field, was figured out for each of the individual experiments, and the sum of the doses on all 4 fields, which thus represent a complete rotation of 360°, were set down in the following scheme. (Fig. 10).

To get the full use of the skin, it was calculated how many degrees past the midline the tube would have to move in order to irradiate the remaining 3 cm. of the surface of the phantom. The distance was found to be 14°, to which correspond 21 sec.; consequently, the irradiation could be kept up for 2 min. 37 sec. without overlapping of the two quadrants (Fig. 11). As in the foregoing, with eccentric rotation, the results of all the 4 quadrants were set down in a scheme, the depth doses being figured out in per cent of the respective skin doses. Eccentric rotation over 104° gave the following scheme:

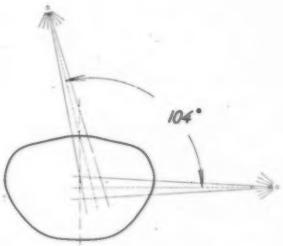

Fig. 11.

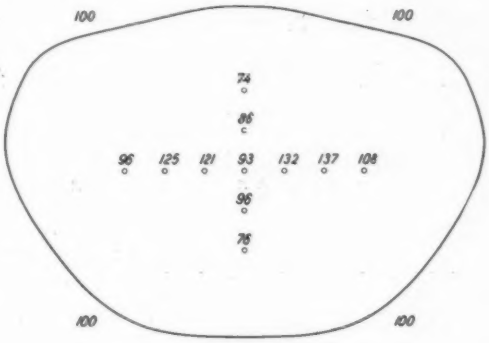

Fig. 12.

Eccentric Rotation with 6 cm. Lateral Displacement

As expected, the eccentric rotation over 104° gave a better depth dose than rotation over 90°, and also the distribution seemed to be better. I therefore tried a rotation with 6 cm. lateral displacement, that is with the axis of rotation corresponding to the pelvic wall. In order to use the skin to the full extent, the rotation was done over 117°, in 2 min. 56 sec. As before, the result of the 4 quadrants was set down in a scheme, the depth dose for each being calculated in per cent of the skin dose and then the figures for all four added together (Fig. 13).

Thus, the eccentric rotation about an axis in each side gives an almost ideal distribution, the dose being largest at the sides, smaller in the center and along the short axis from front to back, corresponding to the cervix, bladder and rectum. One has the impression that also the distribution on the skin is fairly uniform, from 190 to 209 r on a quadrant

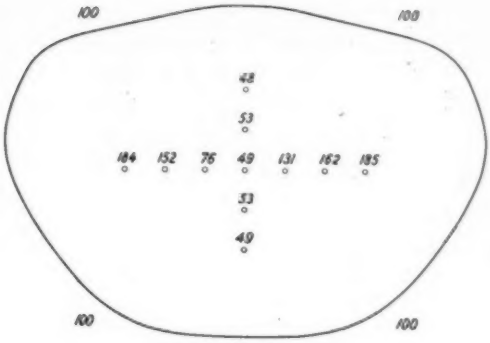

Fig. 13.

irradiated for 4 × 2 min. 56 sec. As there were so few measuring points it was not possible to plot isodose curves, as done by ARNESON & QUIMBY and FLAX; but I believe that the values found may nevertheless be of practical importance. Though the eccentric rotation method is somewhat more laborious and less economic than the method of simple rotation about a single axis in the midline, it is the intention to adopt it for the treatment of future cases of cervical cancer.

SUMMARY

With a view to the combined roentgen- and radium treatment of cervical cancer, the author has done a series of dosis measurements on anatomic phantom, with different fields. Almost the same depth dose is obtained with 2 large fields as with 4 or 8 small, and the distribution is more even.

With rotatory irradiation, both a large depth dose and an even distribution are obtained. The method was therefore chosen as suitable for the purpose. The skin dose and the depth dose obtained by simple rotatory irradiation, with the tube rotating about an axis in the midline were measured on a special paraffin wax phantom of the pelvis.

Along the short axis of the pelvis, the dose was found to be nearly the same in the center as on the skin; but to both sides, along the long axis, there was a considerable diminution. On the skin, the dose was highest in the midline, and diminished about 20 per cent to both sides of the latter.

Double rotation, with oblique adjustment of the tube from above and below and irradiation of two belts, one beside the other, gave a considerable increase of the depth dose; and by increasing the speed in the middle sector, a better distribution in the depth was obtained. But the object aimed at, — namely to obtain the largest dose at the sides — was only obtained by eccentric rotation about an axis on each side, corresponding to the parametria or the pelvic wall.

ZUSAMMENFASSUNG

Im Hinblick auf die kombinierte Röntgen- und Radiumbehandlung des Zervixkrebses hat Verf. Serien von Dosismessungen mit verschiedenen Feldern an anatomi-

schem Modell vorgenommen. Beinahe dieselbe Tiefendosis erhält man bei 2 grossen Feldern wie bei 4 oder 8 kleinen, und die Verteilung ist gleichmässiger.

Bei Rotationsbestrahlung erhält man sowohl grosse Tiefendosis als auch gleichmässige Verteilung. Diese Methode wurde deshalb als zweckmässig gewählt. Die Hautdosis und die Tiefendosis, die man mit einfacher Rotationsbestrahlung erhielt, wobei die Röhre um eine Achse in der Mittellinie rotierte, wurden an einem speziellen Paraffinwachs-Modell des Beckens gemessen.

Längs der kurzen Achse des Beckens erwies sich die Dosis im Zentrum beinahe als die gleiche wie auf der Haut, aber zu beiden Seiten, längs der langen Achse war sie bedeutend vermindert. Auf der Haut war die Dosis in der Mittellinie am grössten und nahm zu beiden Seiten von derselben um 20 % ab.

Doppelte Rotation mit schräger Einstellung der Röhre von oben und unten und Bestrahlung zweier Streifen neben einander ergab eine bedeutende Zunahme der Tiefendosis und durch Vergrösserung der Schnelligkeit im Mittelsektor erhielt man eine bessere Verteilung in der Tiefe. Aber das erstrebte Ziel — die Erreichung der höchsten Dosis an den Seiten — konnte nur durch exzentrische Rotation um eine Achse auf jeder Seite, die dem Parametrium oder der Beckenwandung entsprach, erreicht werden.

RÉSUMÉ

En vue d'étudier les conditions du traitement combiné du cancer du col par Rayons Roentgen et Radium l'auteur a fait une série de mesures dosimétriques sur un mannequin en utilisant différents champs. On obtient presque la même dose dans la profondeur avec deux grands champs qu'avec 4 ou 8 petits, et la répartition est plus égale.

Avec l'irradiation rotatoire on obtient à la fois une forte dose dans la profondeur et une répartition régulière. Aussi cette méthode fut-elle choisie comme adéquate au but poursuivi. La dose cutanée et la dose profonde, fournies par simple irradiation rotatoire, avec le tube tournant autour d'un axe sur la ligne médiane, furent mesurées sur un mannequin spécial en cire représentant le bassin.

Le long du petit axe du bassin la dose se montra, à peu de chose près, la même au centre qu'à la peau; mais sur les deux côtés, le long du grand axe, la diminution était considérable. A la peau la dose atteignait son maximum sur la ligne médiane, et de part et d'autre de celle-ci elle diminuait d'environ 20 %.

La double rotation, avec ajustement oblique du tube, d'en haut et d'en bas, et irradiation de deux ceintures, l'une à côté de l'autre, procura un accroissement considérable de la dose profonde, et en augmentant la vitesse du secteur moyen on gagna une meilleure répartition dans la profondeur. Mais le but poursuivi — à savoir d'obtenir la dose la plus grande sur les côtés — ne fut atteint que par une rotation excentrique autour d'un axe de chaque côté, correspondant aux paramètres ou à la paroi du bassin.

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FROM THE ROENTGEN DEP'T OF THE FREDERIKSBERG HOSPITAL, COPENHAGEN
(CHIEF: BØRRE LARSEN, M. D.)

SOME CASES OF INTESTINAL TUBERCULOSIS IN PHTHISICS, WITH REFERENCE ESPECIALLY TO THE PROGNOSIS[1]

by

Sv. Børre Larsen

The object with the present communication has been to study the course of the tuberculous, ulcerous enterocolitis that occurs secondarily to pulmonary tuberculosis, and which it has been possible to control by after-examinations from three to eight years after the diagnosis had been established roentgenologically. The work was taken up especially on account of the strictures which occurred later, owing to cicatricial shrinkings. The fact is that between the primary intestinal tuberculosis, where the patient becomes infected with tubercle bacilli in the intestine through food or the like, while there is no tuberculosis of other sites, and the secondary, where a phthisic infects his intestinal tract by swallowing sputum containing the bacilli, there is the difference that the former often gives rise to strictures, which may be solitary or multiple, while the latter should seldom result in the formation of cicatrices with annular strictures. Without entering into pathoanatomical details it may be mentioned that both KAUFMANN and BRUNNER at necropsies on patients who had died from primary intestinal tuberculosis found strictures in a large number of cases. As most cases of secondary intestinal tuberculosis occur in the late stages of pulmonary tuberculosis, it is possible that cicatricial shrinking does not get time to develop before death sets in. Not a few patients get cured, however, of both their pulmonary and their intestinal tuberculosis. The present study deals with patients whose intestinal tuberculosis has been cured or bettered, and whose pulmonary tuberculosis has not been of such a character that it has resulted in the patient's death during the observation time. Therefore, only a few of the diagnoses are verified by necropsy. Two of the patients died

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later, however; and in these cases the necropsies showed the results of tuberculous, ulcerous processes in the cecum and ascending colon. One patient was operated upon, and his appendix removed; and microscopy of the latter showed tuberculous changes in the tissue.

Secondary intestinal tuberculosis most often has its seat in the caudal loops of the ileum and in the cecum and ascending colon; especially are the two last-named sections of the gut a frequent site. It has been thought that this might be because PAYER's plaques are more pronounced there than in the other sections, but perhaps it is rather because the contents of the gut which contain the tubercle bacilli remain in contact with the mucosa of the intestinal wall for a longer time there than in the other parts (LAWRASON, BROWN & SAMPSON). Of the many statistics which show how frequent the complication is, I shall cite only ENGELMANN's, according to which it is found in about 92 per cent of the cases of pulmonary tuberculosis that come to necropsy. Other statistics give a somewhat lower figure, however. It is probable, though, that there in these analyses has been question of patients whose death was due to advanced pulmonary tuberculosis; and as the number of cases of intestinal tuberculosis increases towards the end of the disease, when the patient's power of resistance is broken, we have here an explanation of the high figures. These reported cases are, of course, of considerable clinical importance; still, the greatest clinical interest attaches rather to the cases which occur in an earlier stage of the disease, because it in these is possible to deal successfully with the complication and thus increase the possibility of curing the pulmonary phthisis.

It was only after the introduction of roentgenologic diagnosis that it became possible to any considerable extent to recognize the presence of a tuberculous, intestinal affection at an earlier stage; namely so early that the patient only presents vague, indefinite symptoms, or no symptoms, at all, of any affection of the intestinal tract and only a disproportion between his general condition and what the latter would be expected to be considering the extent and character of his pulmonary affection suggests a possible complication from the intestine. The material here presented consists of 32 cases, all of patients with bacillary pulmonary phthisis complicated by enterocolitis; the diagnosis of the latter having been established by roentgen examination at the earliest possible stage; that is at the occurrence of the first symptoms or at a time when the patient's general condition gave grounds for suspecting the presence of the said complication.

The procedure has been the one usually employed in recent years, of administration of a contrast meal, followed by fractioned roentgen examination by screening and exposures beginning 4—5 hours after, and continued until the contrast substance has passed the different por-

tions of the gut. If there is marked hypermotility, the hours for the inspection must often be changed and the whole examination begun earlier.

The method of the examination builds on descriptions of examinations of intestinal tuberculosis published, in 1919, by LAWRASON, BROWN & SAMPSON. But also before that time several studies on the diagnosis of that affection had appeared. Thus, STIERLIN published in 1911 his studies on ileocecal tuberculosis and described the symptom, since named after him, which consists in the absence of contrast substance in that portion of the gut, even when there are accumulations of it both orally and anally to it. Later investigations have shown, however, that STIERLIN's symptom is not an invariable one; thus, FAULHABER published, in 1914, two cases of indubitable ileocecal tuberculosis in which it was not present, but in which there was a pathologic diminution of the ascending colon and local hypermotility. Also FLEMMING MØLLER has published a study, in 1922, in which he came to the conclusion that the presence of STIERLIN's symptom was not necessary in order to establish the diagnosis of ileocecal tuberculosis.

Other investigators, for instance FLEISCHNER & BRONCHHORST, have chiefly used passive filling of the colon by means of contrast enema, if necessary supplemented by insufflation of air (FLEISCHER); but in our opinion serial inspections after contrast meal are absolutely the best method, because it gives better information about the motility of the intestine and other physiologic conditions than the passive distention with contrast enema; not to speak of the possible risk of perforation if there are extensive, deep ulcerations. GERSHON-COHEN & SHAY have, however, in 1939 published another method, namely enteroclysis through a duodenal sound, if necessary combined with insufflation of air through the latter after it has been ascertained, by screening, that the contrast enema has passed through the small intestine. They claim that a result is obtained more quickly by this method, because the contrast fluid passes all the way down to the colon already after a few minutes, and very rapidly fills it for the whole distance over to the left flexure. Besides thus making it possible to establish the diagnosis in very short time, the method has the advantage that with the insufflation of air one gets a good picture of the mucosal relief. The examinations by means of contrast meal may often with good result be combined with opaque enema; what was also done in one of the cases in the present material.

FLEMMING MØLLER was the first Danish author to publish a study on roentgen examination in early intestinal tuberculosis. In this paper, which was written in collaboration with H. C. GRAM and appeared in 1929, also the peroral method is used. Later, studies of the subject have been published by CHRISTIANSEN and others.

In 1938, TISELL published a large work on the early diagnosis, with many reports of cases that had come to necropsy, at which the diagnosis and the roentgenologically found locations had been verified. The necropsies were performed after postmortem fixation with formalin *in situ*, and the roentgen examination made after the removed section of the gut had been filled with contrast substance. Not until this had been done was the preparation examined histologically, at which examination TISELL found that the filling defects were due to foldings of the mucosa, which alone are determining for the roentgenologic appearance of the intestine; a finding which accords with FORSSELL's theories about the autoplasticity of the mucosa.

The roentgenologic symptoms on which the diagnosis builds are (1) changes in the motility and (2) the presence of local filling defects. Of course, these symptoms are not pathognomonic for a tuberculous affection of the intestine; but when it is a question of local changes at the ileocecal junction in a patient with bacillary phthisis, it is highly probable that they are indications of precisely such an affection.

(1). The change in the motility may express itself either in excessive or in diminished movement. The former is the most frequent, and may be either general or local. It is fairly easy to diagnosticate roentgenologically. If there is general hypermotility, the colon is seen to empty in shorter time than the normal 36—48 hours after the ingestion of the contrast meal, and the opaque substance is often found in its caudal portion already after a few hours. In case of local hypermotility, the caliber of the affected portion of the intestine will be smaller than normal, increasing to complete void of contrast (STIERLIN's symptom). Hypomotility expresses itself clinically in the relatively frequent obstipation in these patients, though its roentgenologic manifestations are rare.

An import symptom of ulcerous changes in the caudal loops of the ileum and in the ileocecal valve is ileostasis, retarded emptying of the ileum. The time at which the cecum begins to fill is stated somewhat variously by the different authors; TISELL says 2 hours, others 3—4 hours, after meal. Also the time after which the ileum should be empty is stated somewhat variously, according to TISELL the normal time should be 8 hours, FLEISCHER and DAWID find 9 hours to be the normal. NOECHEL even sets 10 hours as the limit within which the ileum should be empty, but his material is chiefly pediatric. DEHN and PANSDORF call attention to the curious fact that emptying of the ileum is retarded during protracted inanition. DEHN examined different patients during the hunger period in Russia an found that the contrast meal remained for up to twenty-four hours in the small intestine. He considers this as simply a compensatory reaction on the part of the organism, which tries by this means to ensure the extraction of as much nourishment as possible.

The writer has examined 100 individuals with sound colon, with regard to emptying of their ileum, and found that in 77 per cent of them it emptied within 9 hours, while in 23 per cent there still was a remnant left at the end of that time. The last figure must be corrected, though; because 7 had not emptied their bowels within the normal time. Thus, there was a remnant left only in 16 per cent, and this remnant was in all cases small.

(2). Filling defects were formerly held to be spastic phenomena (and »finger-pressure spasms»); but these concepts need hardly be considered here, since it must be taken for proved that FORSSELL's theory is correct, according to which they are due to strong folding of the mucosa as result of a co-ordination of muscular and vasomotoric (hydrodynamic) influences. TISELL found in his investigations that »the thickness of the folds was essentially determined by inflammatory edema or by displacements of fluids, congestion in the submucosa, which latter in all the cases exhibited greatly dilated vessels.» The strong folding of the stomach must, according to FORSSELL, be conceived as a mechanism of protection, similar to what is known from duodenal and gastric ulcer, preventing the contents of the gut from coming into contact with the ulcerations themselves. The defects may vary from one time to another, but must nevertheless be said to be fairly constant.

Besides the symptoms named, there may also be changes in the peristalsis of the intestine in the form of a much more frequent mass peristalsis than normal, beginning in the distant half of the transverse colon (FLEMMING MOLLER). Corresponding to this, the haustra are seen to become effaced; but they may form again when the movement is ended. As a rule, the haustration will not be seen in cases of ulcerative processes, however. On the other hand, the occurrence of haustra does not exclude the presence of ulcerations; BROWN & SAMPSON have seen normal haustration in proved cases of such. This applies chiefly to the distal portion of the colon.

When there in connexion with local ulcerative processes in the colon or ileum either occurs »spasms» and local hypermotility, or, in other cases, general hypermotility, perhaps in connexion with local spasms, it may be due to the strength of the irritation and certain peculiarities in the patient.

The present material consists of 32 cases, in all of which there were bacillary pulmonary changes of one kind or another. They were selected from a larger number, having survived so long after the diagnosis had been made, that the observation time was of suitable length. In 8 of them, the pulmonary changes were chiefly exudative ones in the parenchyma; the other 24 presented the picture of exudative, proliferative changes. Quite apart from the patient's allergic condition in other respects, it

might with some reason be supposed that patients who excreted many tubercle bacilli were the ones particularly liable to autoinfection in the intestine, and it was therefore to be expected that there would be a large number with degenerative processes in the lungs. KLINE, who has studied the relationship between the different processes in the latter and tuberculosis of the intestine, found the last-named complication most frequent in connexion with cavernous phthisis. GARDNER found cavern formations in the lungs in 52 per cent of cases, and similar figures were found by BOELS. GERSHON-COHEN has published the results of 226 necropsies, and finds that intestinal tuberculosis is most frequent in connexion with ulcerous, cavernous phthisis. In the present material, there were cavernous changes in the lung in 14 of the cases (about 45 per cent) at the time when the roentgen examinations of the intestine were made. Some others became cavernous at a later period, though.

Of other tuberculous manifestations that occurred simultaneously with the intestinal tuberculosis may be mentioned tuberculous laryngitis, which occurred only in 1 case, however (Case no. 25). Tuberculous pleuritis occurred in 3 cases (nos. 26, 28 and 29). One patient had tuberculous osteitis of the leg.

The length of the interval between the time when the pulmonary tuberculosis declared itself and the appearance of the first symptoms of the intestinal complication varied considerably. In 3 cases (nos. 14, 20 and 28) the symptoms from the intestine are seen to have been present at the time when the patient's pulmonary phthisis was revealed. The longest intervals were in the cases no. 16 (6 years), no. 8 (2 years), no. 25 (3 years) and no. 30 (4 years). In all the other cases the interval was from about 3 to 8 months.

The clinical symptoms which directed the attention to the presence of a tuberculous enterocolitis were in 12 cases diarrhea, in 2 obstipation, in 11 cardialgia, in 4 nausea, in 4 indefinite abdominal pains, in 1 vomiting, and in 1 bleeding from the anus. In 8 cases there were no actual dyspeptic symptoms, but an inconsistency between the patient's general condition and the pulmonary findings.

Triboulet's test was made in 22 cases. In 15 the reaction was positive, varying from + to +++; in 7 it was negative. It was thus positive in about 70 per cent, which agrees more or less with what has been found by HERTZBERG, TISELL and other investigators. The blood sedimentation reaction at the onset of the intestinal tuberculosis was extremely various. In most of the cases rather high values were found, up to 101 mm./h.; most of them lay about 40—50 mm./h, one was as low as 5 mm./h.

The roentgenologic symptoms on which the diagnosis was based were the usual. Hypermotility was found in 23 cases, filling defects in 32, ileostasis in 15, positive STIERLIN symptom in 1. In 28 cases, the ulcerous

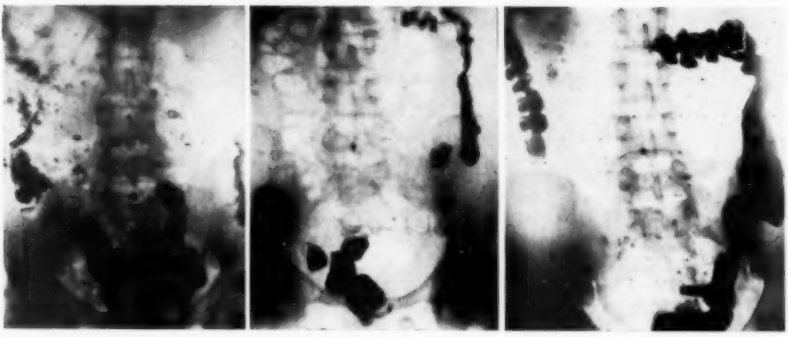
changes were confined to the cecum and the ascending colon, in 4 there were signs of ulceration also in the caudal loops of the ileum.

All the patients were given all-over carbon-arc light treatment, one of them (case no. 27) also a roentgen treatment by BACHMEISTER's method. The treatments were given in series of 60—100 sittings, in most of the cases with good effect, as evidenced by increase in weight, better appetite and fall in the blood sedimentation rate. Roentgen examinations some time after ended treatment showed in 17 complete cure of the intestinal tuberculosis, with return to normal conditions. In 12 cases there was improvement, but still some signs of tuberculous manifestations in the gut; only 3 cases showed no improvement. In some of the cases there was, however, between the first examination and the control examination, a recurrence of the intestinal affection, for which renewed treatment was given.

All the cases have been followed up, but in 11 of them the present situation has made it impossible for the patient to present himself in person for after-examination, and in these we have had to content ourselves with a written communication about the subjective condition. In the other 21 cases we have been able to ascertain the present condition in the intestinal tract by roentgen examination after ingestion of contrast meal, and the cases may therefore be divided into two groups.

1. *Cases after-examined roentgenologically.* The interval between the first examination and the after-examination was in 2 of these cases (nos. 1 and 17) 8 years, in 4 (nos. 2, 3, 8 and 15) 6 years, in 2 (nos. 25 and 29) 5 years, in 9 (nos. 4, 10, 11, 14, 16, 20, 27, 31 and 32) 4 years, in 3 (nos. 22, 26 and 28) 3 years, in 1 (no. 24) 2 years. In 3 cases (nos. 2, 4 and 31) the examination showed entirely normal conditions, in other words complete cure of the intestinal tuberculosis. In 2 cases (nos. 1 and 3) there was granular hypertrophy, in 7 (nos. 17, 20, 22, 24, 25, 29 and 32) cicatricial changes about the ileocecal valve, in the form either of semilunar rarefactions about the valves themselves or of rigidity of the adjoining intestinal wall. In 3 cases (nos. 11, 14 and 15) there was ileostasis lasting for over nine hours; in one of these (no. 15) for over twenty-eight hours after meal. In 2 cases (nos. 26 and 28) there were signs of cicatricial changes in the caudal loops of the ileum, partly in the form of irregular configuration of a portion of the loops, partly in the form of a constantly narrowed portion of the latter. In 5 cases (nos. 8, 10, 16, 27 and 28) signs of fresh ulcerous changes were found in the cecum and the ascending colon.

Thus, the result of the after-examination showed entirely normal conditions only in 3 of the 21 cases, while in the rest there were distinct changes. With a few exceptions, the after-examined patients presented no subjective symptoms. They felt well, there was no dyspepsia, and in most of them the processes in the lung had subsided. The only exception to this was case no. 15, in which there later developed a recurrence in the



First examination. After 4 years. After 8 years.

Fig. 1.

cecum and the ascending colon. There were no actual dyspeptic symptoms, but the patient continued to lose weight, the processes in the lung became graver, and a year after the after-examination she died after a hemoptysis.

2. *Follow-up, not controlled by roentgen examination.* This group is of less interest, because the statements respecting the condition are based only on the patients' subjective estimate. The interval between the first examination and the time when these statements were made was in 1 case 12 years, in 2 cases 11, in 1 case 9, in 1 case 8, in 1 case 7, in 1 case 6, in 2 cases 5, and in 2 cases 3 years.

Case Histories

Case 1. Man, 21 year old, admitted to tuberculous ward of the Frederiksberg Hospital with extensive exudative changes in the right lung. Blood sedimentation rate, 18 mm./h. Sputum positive for tubercle bacilli. First roentgen examination of colon: typical changes in the cecum and ascending colon. Light bath treatment, resulting in 2.2 kg. increase in weight. Dyspepsia. In the following years the patient was in sanatorium and at home. After 2 years, aggravation of the processes in the lung. Second roentgen examination of the colon: typical tuberculous changes in the ascending portion and in the caudal loops of the ileum. Dyspepsia. Again light bath treatment, resulting in improvement. Third roentgen examination of the colon: no change. In the following year no dyspepsia; now and then slight diarrhea. Four years after first admission admitted again, with cavernous phthisis. Fourth roentgen examination of the colon: general hypermotility, without haustration with irregular mucosal relief. Five years after the first admission a fifth roentgen examination of the colon showed general hypermotility and, in the cecum and ascending colon, chronic, proliferative processes. Three years later (8 years after the first examination), a sixth roentgen examination showed the colon transformed into an apparently rigid tube without haustra, with hypermotility and granular hypertrophy. The processes continued to develop, and 9 years after the first admission the patient died. No necropsy. (See Fig. 1.)

Case 2. Woman, 21 years old, admitted to tuberculous ward of the Frederiksberg Hospital with extensive infiltrative processes in the right lung, of exudative, proliferative character. Three months later, diarrheas. First roentgen examination of the colon: typical changes in the distal loops of the ileum, the cecum and the ascending colon. Light baths (35). Two years after, second examination of colon: no signs of colitis. Sedimentation rate, 4 mm./h. Triboulet, negative. Follow-up examination 5 years later showed condition in the intestine entirely normal. No dyspeptic symptoms.

Case 3. Woman, 30 years old, admitted to tuberculous ward of the Frederiksberg Hospital with tuberculosis of the right lung, of exudative, proliferative character, with incipient degeneration. Sedimentation rate, 86 mm./h. Sputum positive for tubercle bacilli. Four months after admission, complaints of pain in the abdomen. Roentgen examination of the colon: typical changes in the ascending portion; positive STIERLIN symptom. Light baths (25). Increase in weight, 3 kg. Sedimentation rate at the end of treatments, 42 mm./h. Second roentgen examination, a year later: condition in the intestine almost normal, only the contours of the cecum and the ascending colon slightly irregular. At the third examination, 6 years after, slight granular hypertrophy of the ascending colon. No changes in motility. Defecation normal. No dyspepsia.

Case 4. Woman, 16 years old, admitted to the tuberculous ward of the Frederiksberg Hospital with fresh exudative changes in the right lung. Sedimentation rate, 9 mm./h. Roentgen examination of the colon, 5 months after admission: filling defects in the cecum and the ascending colon. Positive hypermotility. Light baths (50), resulting in increase of weight, 8.5 kg. No dyspepsia. Second roentgen examination of the colon, 2 years later: no signs of tuberculous changes. Third examination, 4 years later: the intestine normal. No dyspepsia.

Case 5. Woman, 18 years old, admitted to tuberculous ward of the Frederiksberg Hospital with extensive tuberculosis, of exudative character, in the left lung. Indefinite pains in the abdomen; therefore roentgen examination of the colon, which showed general hypermotility, and filling defects in the ascending portion. Light baths (26); increase in weight. 3.5 kg. Fall in sedimentation rate, to 16 mm./h. No dyspepsia. Second roentgen examination, at the end of light bath treatments: intestinal affection cured. Follow-up, 7 years later (no roentgen examination): No dyspepsia; defecation normal.

Case 6. Woman, 23 years old, admitted to tuberculous ward of the Frederiksberg Hospital with extensive, proliferative processes in both lungs, with cavern in side. In the course of a year increasing dyspepsia, and diarrhea alternating with obstipation. Roentgen examination of the colon showed general hypermotility, filling defects and ileostasis lasting 32 hours. Light baths (61); increase in weight. 6.4 kg. Second roentgen examination, 7 months later: conditions normal, the ileum empty 9 hours after meal. Control examination 5 years later: conditions in intestine normal; no dyspepsia.

Case 7. Woman, 31 years old, admitted to tuberculous ward of the Frederiksberg Hospital with extensive exudative processes in the left lung. Stools thin. A month after admission suddenly copious bleeding from rectum. First roentgen examination of colon: filling defects corresponding to the cecum, and ileostasis. Light baths (40). Sedimentation rate constantly low (5 mm./h.). Follow-up 12 years later (no roentgen examination): Feces stated to be rather hard; otherwise no dyspeptic symptoms.

Case 8. Woman, 40 years old, admitted to tuberculous ward of the Frederiksberg hospital with extensive exudative, proliferative processes in both lungs, + cavern.

Sedimentation rate, 50 mm./h. Diarrhea. Roentgen examination of the colon: general hypermotility, filling defects about the ileocecal junction. Light baths (26); increase in weight, 1.6 kg. Again admitted 5 years later, for dyspepsia and strong diarrheas. Varying filling defects and local hypermotility in the cecum and ascending colon. Triboulet reaction +++. Five years later, third roentgen examination of the colon: the cecum and ascending colon narrow, with local hypermotility. Six months later the patient died. Necropsy showed tuberculous ulcers in the large intestine.

Case 9. Man, 20 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative, proliferative processes in the left lung, nausea and vomitings. Had been in the Oeresunds Hospital, Copenhagen, 4 years previously, also for tuberculosis. Sedimentation rate, 32 mm./h. Roentgen examination of the colon showed filling defects in the cecum and ascending colon. Light baths (40); increase in weight, 3.5 kg. Follow-up 3 years later (no roentgen examination): Well-being; no signs of colitis.

Case 10. Woman, 28 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative processes and caverns in both lungs. Diarrhea and cardialgia. Roentgen examination of the colon: filling defects and ileostasis. Light baths (60); increase in weight. 4.5 kg. No dyspepsia. Second roentgen examination, 5 months later: improvement. Third roentgen examination, 4 years later: still filling defects in the cecum and ascending colon, and ileostasis. Follow-up, 3 years later (no roentgen examination): No dyspepsia; no signs of intestinal tuberculosis.

Case 11. Girl, 5 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative, proliferative processes and cavern formation in left lung. Cardialgia, nausea, periodic diarrhea, and positive Triboulet reaction. Roentgen examination of the colon: filling defects in the cecum and ascending colon, hypermotility and ileostasis. Light baths (40); dyspepsia less pronounced. Roentgen examination of the colon 5 months later: no filling defects, but slight ileostasis and thickenings corresponding to the ileocecal valve. Control-examination 4 years later: still slight ileostasis, but conditions otherwise normal.

Case 12. Woman, 37 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative, proliferative phthisis of both lungs. Three years prior to admission, pleuritis. Sedimentation rate, 80 mm./h. Triboulet, negative. Patient sent to roentgen examination on account of poor general condition. Filling defects corresponding to the cecum and ascending colon, + ileostasis, found. Light baths (45). Sedimentation rate falls to 20 mm./h. Increase in weight, 9 kg. Roentgen examination of the colon 5 months later: conditions normal. Follow-up, 5 years later; some obstipation; otherwise nothing abnormal.

Case 13. Woman, 32 years old, admitted to tuberculous ward of the Frederiksberg Hospital with bilateral exudative, cavernous phthisis. Cardialgia, diarrhea and Triboulet reaction +++; therefore roentgen examination of the colon, which showed filling defect in the ascending portion and hypermotility. Light baths (60); increase in weight, 7.3 kg. Fall in sedimentation rate from 85 to 17 mm./h. Roentgen examination of colon 6 months later: conditions normal; Triboulet reaction negative. Follow-up, 3 years later: Well-being; no dyspepsia.

Case 14. Man, 40 years old, admitted to tuberculous ward of the Frederiksberg Hospital with extensive exudative, proliferative processes in the lungs. Sedimentation rate, 58 mm./h. On account of poor general condition roentgen examination of the colon:

general hypermotility; typical tuberculous changes in the cecum and the caudal loops of the ileum. Light baths (68); increase in weight, 16 kg. Roentgen examination of the colon 10 months later: conditions normal. Control-examination 4 years later: slight ileostasis 9 hours after meal, and contour of the ileum slightly irregular; the cecum normal. Follow-up 3 years later (no roentgen examination): Triboulet negative. No dyspepsia.

Case 15. Woman, 26 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative, proliferative tuberculosis of both lungs. Some obstipation. Sedimentation rate, 16 mm./h. Roentgen examination of the colon: filling defects in caudal part of the ileum, in the cecum and the ascending colon, + hypermotility. Light baths (51); increase in weight, 2 kg. Second roentgen examination, 5 months later: the ileum normal, but still filling defects in the cecum and the ascending colon. Third roentgen examination, 22 years later: conditions in intestine normal. Fourth examination; 7 years later: considerable ileostasis for more than 28 hours after meal; contours of the cecum and the ascending colon rather irregular. The patient died a year afterwards.

Case 16. Boy, 16 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative, proliferative tuberculosis of both lungs. Six years previously slight pulmonary tuberculosis. Sedimentation rate now 36 mm./h. Triboulet negative. On account of cardialgia roentgen examination of the colon: filling defects in the cecum and in the ascending and transverse colon. Light baths (72). Second roentgen examination of the colon, 6 months later: conditions normal. Third examination, 4 years later: again signs of filling defects in the cecum and the ascending colon, + hypermotility. Again light baths; the sedimentation rate falls to 4 mm./h. Follow-up 3 years later: Well-being; no dyspepsia.

Case 17. Woman, 23 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative, proliferative tuberculosis of both lungs. Sedimentation rate, 30 mm./h. Triboulet + +. On account of diarrhea roentgen examination of the colon: filling defects in the cecum and ascending colon; hypermotility; ileostasis. Light baths (47); increase in weight, 7 kg. Fall in sedimentation rate to 20 mm./h. Two years later, second roentgen examination of the colon: considerable improvement. Third examination 3, years later: normal passage; semilunar defects in the barium shadow corresponding to the ileocecal valve, owing to cicatricial changes. No dyspepsia.

Case 18. Woman, 25 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative, proliferative processes in both lungs. Sedimentation rate, 25 mm./h. No dyspepsia. On account of poor general condition roentgen examination of the colon: filling defects and ileostasis. Light baths (43); increase in weight, 4 kg. Second roentgen examination, 14 months later: considerable improvement. Third examination, 2 years later: nothing abnormal in the cecum or the ascending colon, but distended ileal loops, and considerable ileostasis 9 hours after meal. Signs of cicatricial changes. No measures taken, however. Follow-up 7 years later (no roentgen examination): defecation normal, no abdominal pains; no clinical signs of stenosis of the small intestine.

Case 19. Man, 21 years old, admitted to tuberculous ward of the Frederiksberg Hospital with extensive exudative, proliferative processes in both lungs. On account of abdominal pains and loss of weight roentgen examination of the colon: distinct filling defects corresponding to the cecum. Triboulet negative. Light baths (87); increase in weight, 7 kg. Fall in sedimentation rate to 10 mm./h. Follow-up 11 years later (no roentgen examination): Well-being; no signs of colitis.

Case 20. Woman, 26 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative processes and caverns in both lungs. Sedimentation rate, 50 mm./h. No sure dyspeptic symptoms. On account of her poor general condition roentgen examination of the colon: filling defects in the cecum, ascending colon and ileum; hypermotility and ileostasis. Light baths (200). Well-being. Roentgen examination of the colon 4 years later: semilunar rarefactions about the ileocecal valve, owing to cicatricial changes. Otherwise, conditions normal. Sedimentation rate, 30 mm./h. Triboulet negative.

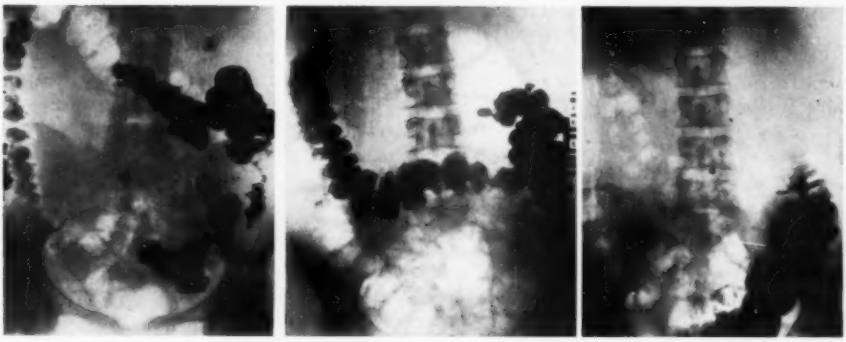
Case 21. Man, 22 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative, proliferative processes in both lungs. After stay in sanatorium and discharge admitted a second time. No dyspeptic symptoms. Roentgen examination of the colon: filling defects corresponding to the cecum and the ascending colon. Second roentgen examination, 5 months later: conditions in intestine normal. No dyspeptic symptoms. Follow-up 11 years later (no roentgen examination): complete well-being.

Case 22. Man, 24 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative, proliferative processes in the left lung. Sedimentation rate, 101 mm./h. Triboulet ++. On account of pains in the abdomen and diarrhea roentgen examination of the colon: filling defects in the cecum and ascending colon, and ileostasis. Discharged to sanatorium. Roentgen examination of the colon 18 months later: cicatricial changes about the ileocecal valve, ileostasis and hypermotility. Sedimentation rate, 32 mm./h. Third roentgen examination of the colon, 2 years later: no filling defects or ileostasis. Fourth examination, 5 years later: signs of cicatricial changes corresponding to the ileocecal valve; ileostasis 9 hours after meal. Two months later, the patient died suddenly, with hemoptysis. Necropsy showed healed tuberculous processes in the ileocecal region, with cicatrices.

Case 23. Man, 55 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative, proliferative processes in both lungs. Sedimentation rate, 35 mm./h. Seven months after admission, roentgen examination of the colon, on account of diarrhea and abdominal pains: filling defects in the cecum and the ascending colon, ileostasis and hypermotility. Light baths (85); increase in weight, 9 kg. Sedimentation rate unchanged. Roentgen examination of the colon 8 months later: filling defects less pronounced; no ileostasis. Follow-up 8 years later (no roentgen examination): defecation normal; no pain or dyspepsia.

Case 24. Man, 24 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative tuberculous processes in both lungs. No dyspepsia. Discharged, and returned 5 years later with extensive exudative, proliferative processes in both sides. On account of cardialgia and obstipation roentgen examination of the colon: filling defects in the cecum and the ascending colon. Sedimentation rate, 75 mm./h. Positive Triboulet reaction. Light baths (64); increase in weight, 9 kg. Roentgen examination of the colon 1 year later: improvement. Third roentgen examination, after another year: signs of slight cicatricial changes in the caudal loops of the ileum.

Case 25. Woman, 25 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative, proliferative processes in the right lung. Discharged, but admitted again 3 years after with largely extended processes in both lungs. On account of cardialgia and diarrhea roentgen examination of the colon, showing filling defects in the cecum, ileostasis and hypermotility. Positive Triboulet reaction. Sedimentation rate, 31 mm./h. Light baths (52); increase in weight, 2 kg. Tuberculous laryngitis. Second roent-



First examination. After 3 years. After 5 years.

Fig. 2.

gen examination roentgen examination of the colon, 2 years later: no filling defects, no ileostasis, no hypermotility. Sedimentation rate, 24 mm./h. Third examination, 5 years after the first: cicatricial changes about the ileocecal valve. (Fig. 2).

Case 26. Man, 48 years old, admitted to tuberculous ward of the Frederiksberg Hospital with tuberculosis, largely proliferative, of both lungs. Sedimentation rate, 5 mm./h. Positive Triboulet reaction. Diarrhea. Roentgen examination of the colon; 1 year after admission: filling defects in the ileum and the cecum. Light baths (53). The diarrhea persists. Second roentgen examination, a year later: no filling defects, but ileostasis 9 hours after meal. After-examination 3 years later: occasional diarrheas and frequent spells of pain in the lower part of the abdomen. Roentgen examination of the colon: the cecum and ascending colon normal; a part of the caudal loops of the ileum constantly narrowed (perhaps a rest of tuberculosis). Clinical examination 11 years later: no dyspepsia or pains.

Case 27. Man, 21 years old, admitted to tuberculous ward of the Frederiksberg Hospital with partly exudative, partly proliferative processes in the lung. Seven months after admission nausea, vomitings and Triboulet +++, wherefore roentgen examination of the colon: filling defects in the cecum, the ascending colon and the ileum; hypermotility. Light baths (44). The pains increase and the diarrhea persists. Roentgen treatment by BACHMEISTER's method tried: 2 séances; 2 fields over the abdomen; distance, 40 cm.; filter, 5 mm. Al.; size of fields, 10×15 cm.; dose, 100 r. The treatment given 3 times, with intervals of 10 days between. Distinct improvement; the diarrheas cease. Patient sent to sanatorium. Again admitted 4 years later, with extension of the processes in both lungs and cavern formation. Third roentgen examination of the colon: filling defects about the ileocecal junction; hypermotility. The stools persistently thin. Triboulet + + +. Sedimentation rate, 20 mm./h. Temperature a little high. Discharge.

Case 28. Woman, 24 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative processes in both lungs, degeneration and left-side pleuritis. Sedimentation rate, 74 mm./h. Positive Triboulet reaction. No dyspepsia. Daily, spontaneous defecation. Roentgen examination of the colon: typical filling defects in the cecum and ileostasis. Light baths (36). Sent to sanatorium. Roentgen examination a year later:

only semilunar rarefactions about the ileocecal valve and slight ileostasis. No dyspepsia. Control-examination 3 years later: again characteristic filling defects in the cecum, the ascending colon and the caudal loops of the ileum. Pain, diarrhea and increased temperature. Triboulet ++. Two years years after, the patient died. The necropsy showed extensive tuberculous ulcerations in the small and the large intestine.

Case 29. Woman, 24 years old, admitted to tuberculous ward of the Frederiksberg Hospital with extensive exudative and proliferative processes in the lungs, with degeneration and pleuritis. No dyspepsia. Sedimentation rate, 45 mm./h. Positive Triboulet reaction. Roentgen examination of the colon, 3 months after admission: typical filling defects in the cecum and the ascending colon; ileostasis 9 hours after meal. Light baths (34); increase in weight, 8 kg. Fall in sedimentation rate to 6 mm./h. Second roentgen examination 4 months later; no filling defects, but hypermotility. Follow-up, 5 years later: rigidity about the iliocecal valve and slight ileostasis 9 hours after meal. No dyspepsia.

Case 30. Man, 34 years old, admitted to tuberculous ward of the Frederiksberg Hospital with extensive exudative processes and degeneration in both lungs. Sent to sanatorium. Again admitted 4 years later, with further extension of the processes in both lungs. Sedimentation rate, 57 mm./h. Diarrheas. Hypermotility. Roentgen examination of the colon: Mucosal relief corresponding to the cecum and the ascending colon irregular. Two weeks after this examination laparotomy with removal of appendix. Microscopy: non-tuberculous changes in the tissue. Follow-up, 4 years later: poor filling of the cecum owing to cicatricial changes. Ileostasis. Subjective well-being.

Case 31. Woman, 24 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative, proliferative processes in both lungs. On account of cardialgia roentgen examination of the colon: hypermotility, filling defects in the cecum. Sedimentation rate, 27 mm./h. Control-examination of the colon 4 years later: conditions normal, no ileostasis. Defecation rather sluggish; no pain.

Case 32. Woman, 18 years old, admitted to tuberculous ward of the Frederiksberg Hospital with exudative, proliferative processes and degeneration in both lungs. Sedimentation rate, 40 mm./h. No complaints of dyspepsia, but owing to patient's lack of appetite roentgen examination of the colon: hypermotility and ileostasis; signs of tuberculous changes in the caudal loops of the ileum and in the cecum. Light baths (43); increase in weight, 7.5 kg. Second roentgen examination of the colon, 6 months after the first: conditions normal; only slight ileostasis. Follow-up, 4 years later: still some ileostasis, and signs of rigidity about the cecum.

SUMMARY

The author has examined 32 patients with bacillary pulmonary phthisis in regard to secondary intestinal tuberculosis, particularly with reference to the prognosis; all the examined having lived so long that the observation time was sufficiently long, — from 2 to 12 years. Only in 3 cases did the roentgen examination after that length of time show perfectly normal conditions. In 8 cases there were cicatricial changes about the ileocecal valve, in 2 cases granular hypertrophy; in 11 cases conditions prevented the undertaking of roentgen examination for control in connexion with the follow-up.

ZUSAMMENFASSUNG

Verf. hat 32 Kranke mit bazillärer Lungenphthise inbezug auf sekundäre Darmtuberkulose untersucht, besonders im Hinblick auf die Prognose, und zwar hatten alle Untersuchten so lange gelebt, dass die Beobachtungszeit genügend lang war — zwischen 2 und 12 Jahren. Nur in 3 Fällen ergab die Röntgenuntersuchung nach dieser Zeitspanne einen vollständig normalen Befund. In 8 Fällen lagen narbige Veränderungen in der Gegend der Ileozökalklappe vor, in 2 Fällen granuläre Hypertrophie. In 11 Fällen machten die Umstände eine Vornahme einer Röntgenkontrolluntersuchung bei der Verfolgung des Kranken unmöglich.

RÉSUMÉ

L'auteur a examiné 32 malades atteints de phtisie pulmonaire pour se rendre compte de l'existence possible d'une tuberculose intestinale secondaire, et surtout pour éclairer le pronostic; tous les sujets revus ont vécu assez longtemps pour permettre une observation de durée suffisante — de 2 à 12 ans. Dans 3 cas seulement, après ce laps de temps, l'examen aux Rayons Roentgen montra un intestin parfaitement normal. Dans 8 cas il y avait des altérations cicatricielles autour de la valvule de Bauhin, dans deux une hypertrophie granuleuse; dans 11 cas, l'état de santé empêcha d'entreprendre un examen radiologique de contrôle, en connexion avec la surveillance post-clinique.

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FROM THE RADIUM CENTER, COPENHAGEN (CHIEF: JENS NIELSEN, M. D.)

ROENTGEN TREATMENT OF MALIGNANT TUMORS OF THE NASOPHARYNX[1]

by

Jens Nielsen

Despite their rarity, the malignant tumors of the nasopharyngeal cavity are of marked interest, radiotherapeutically. In the great majority of cases they have been found to be tumors of immature histologic structure, capable of rapid proliferation and with a tendency to early metastasising; but also markedly radiosensitive. Though many attempts have been made to deal with them operatively, no reports exist of cures by surgical procedures; whereas radiotherapy in the last ten years or so can show some lastingly symptom-free cases. There therefore seems to be justification for considering the surgical treatment of these neoplasms as obsolete and characterising them as an exclusively radiotherapeutic domain.

From this it follows that the radiotherapeutist should be thoroughly familiar with the biology and clinical features of these tumors and is under an obligation to deepen our knowledge about them, at the same time as the radiation treatment is worked out to its utmost potentialities for service. Considered from this point of view, the present communication of a not inconsiderable number of cases treated exclusively by radiation therapy and personally observed may perhaps not be without interest.

Author's Material

The present study is based on 77 cases of malignant nasopharyngeal tumors observed at the Radium Center in Copenhagen in the years 1931—1941. All the cases referred to us and diagnosticated during that period are included. None were refused or have been eliminated. For 75 of them there is histologic verification of the cancer diagnosis; the 2 in which no microscopic examination was made were clinically beyond

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doubt, and both patients died of progressive tumor. In all the cases, the treatment was exclusively radiologic, by fractioned irradiation with roentgen.

How rare these neoplasms are, is shown by the fact that the 77 cases constituted less than 1 per cent (0.75 per cent) of the total number of 10,721 cases of malignant affections of all sites treated during the period in question.

Sex- and Age Incidence. — About three-fifths (46) of the patients were men, only two-fifths (31) women. As regards the results of the treatment, there was no surely demonstrable difference between the sexes. The age incidence will appear from Fig. 1. All age classes are represented, from puberty upwards. The youngest patient was 16 years old, the oldest 76. The mean of age can be counted to fully 50 years (52.4). It is worth noting that the younger age classes are not exempt from these tumors, but account for no small proportion of the cases. Seven patients (9 per cent) were under 30, 16 (21 per cent) under 40, 3 under 20 years of age.

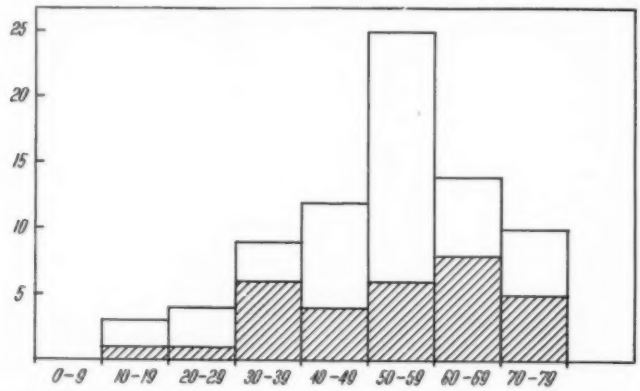

Fig. 1. — Distribution by Age and Sex of 77 Cases of malignant nasopharyngeal Tumor. — Hatched columns; women: blank columns: men.

Nor yet for the roentgenologic prognosis does the question of age appear to play any noticeable rôle.

Symptomatology

Clinically, the nasopharyngeal tumors present several characteristic features, which it is worth knowing, not least for the sake of the early diagnosis. The primary tumor in the nasopharyngeal cavity is in many

cases not very voluminous or exophytic. It may even to all appearances be very small; but the tumors have a marked tendency to early penetration in depth, and to invade the surrounding structures and extend through the lymph channels. The direct symptoms from the nose and pharynx are therefore often entirely overshadowed by syndromes from the cranial nerves, the eyes, the ears or the lymph nodes in the neck, which dominate the clinical picture; and the latter may become very polymorphous, bizarre and misleading.

A particular characteristic is the tendency of the tumors to *invasion through the base of the skull*, leading to *symptoms from the cranial nerves*. This invasion usually takes place through the ~~jugular~~ foramen, but there are also examples of its having taken place by direct penetration of Blumenbach's clivus or the body of the sphenoid bone. Often more or less extensive osseous destructions are caused in the floor of the middle cranial fossa and of the apex of the pyramid, which can be demonstrated by roentgen examination, best in half-axial views of the base of the skull, on LYSHOLM's cranial table. Such roentgenologically demonstrable osseous destructions existed in 26 (34 per cent) of our cases.

When the tumour once has penetrated through the base of the skull, it spreads, especially in the middle cranial fossa, and may there by pressure or invasion give rise to symptoms from a number of cranial nerves in the most different combinations. The sixth cranial nerve, which, owing to its long intracranial course, is particularly vulnerable, is usually the first to become involved. In 4 of our cases, diplopia owing to unilateral paralysis of the abducent nerve was the symptom which caused the patient to seek medical advice. Almost as frequent were, in our material, lesions of the sensitive trigeminus branches (neuralgia, paresthesia, hyperalgesia); in some cases perhaps extracranial, but in most of them due to lateral extension of the tumor around the gasserian ganglion. In 8 cases the patient stated that trigeminus pain had been the first symptom, and in 11 it had been the symptom which caused the patient to consult a physician. By extension more anteriorly, the trochlear, oculomotor and optic nerves become involved; by extension posteriorly, the acoustic seldom, the facial nerve more often. If the invasion of the neoplastic tissue continues farther backwards, also the posterior cranial nerves in the jugular foramen may become involved, leading to paralysis of the palate and fauces. Besides, these nerves may also, like trigeminus II and III, become involved extracranially, either by direct extension of the tumor or through metastases in lymph nodes in the vicinity of the jugular foramen.

In 25 of 64 patients of the present material (40 per cent), GODTFREDSEN found neurologic symptoms during the course of the disease; most often paralysis of the abducent nerve (17 cases) and irritation of the

a. b. c.

Fig. 2. — Development of neuro-ocular symptoms in a man, aged 66 years, with lymphoepitelioma of the nasopharynx and bilateral metastases to the lymph nodes in the neck. — a: when referred to the Radium Center: Horner's syndrome in right eye, due to lymph node compression of the n. sympathicus. — b: 18 months after irradiation with roentgen: paralysis of right abducent nerve, as expression for recurrence with invasion of the tumor tissue through the right side of the base of the skull. — c: 6 months later; in spite of renewed irradiation, the intracranial tumor growth has progressed; there is now ptosis in the right side and complete external and internal ophthalmoplegia.

trigeminus (16 cases). The optic nerve was injured in 4 cases, the oculomotor in 8, the trochlear in 6, the facial in 7, the glossopharyngeal and vagus nerves in 9, the accessory in 2 and the hypoglossal in 2. Bilateral lesion of the same cranial nerve was found in 28 cases. Most of the patients with neurologic symptoms had multiple nerve lesions; in all, 101 nerve lesions were demonstrated in these 25 patients.

In one of our cases, marked permanent *diabetes insipidus* developed, no doubt due to tumor lesion of the posterior lobe of the hypophysis.

Signs of increased intracranial pressure (choked disk) do not, as a rule, develop until in a late stage of the disease; probably because the tumor growth for a long time does not advance beyond the outer side of the dura mater.

Direct invasion of the orbit, with resulting exophthalmus, may occur either from the middle cranial fossa through the superior orbital fissure, or — when the tumor tissue has penetrated through the sphenopalatine fossa — through the inferior orbital fissure. *Horner's syndrome* is, as a rule, produced by pressure of lymph node metastases on the sympathetic in the neck. It was present in 8 of our patients.

The *middle ear* as a rule becomes involved through occlusion or compression of the pharyngeal ostium of the eustachian tube. The usual

Fig. 3. — Voluminous unilateral lymph node metastases in the neck, from a small nasopharyngeal tumor (lymphepithelioma), which had not produced any symptoms, in a young woman, aged 17 years. — After irradiation with roentgen they disappeared completely.

symptoms of occlusion of the tube are the resulting reduced hearing on one ear or both, and a feeling of fullness in the ear or tinnitus. In 4 cases suppurating otitis media developed; in one of these there was also paralysis of the facial nerve, owing to destruction, by the tumor, of the facial nerve in the facial canal. The tumor tissue had in this case invaded the middle ear through the eustachian tube, and had extended its growth out through the perforation in the tympanon, so that biopsy could be done from tissue in the bottom of the external auditory meatus. Symptoms from the ear were in 12 cases the patients' first complaint and in not less than 21 cases what first made them go to the doctor.

Lymph node metastases in the neck frequently occur early in the disease and may reach a considerable size without the primary tumor in the nasopharynx manifesting itself (Fig. 3). In our material we find that swelling of one or several lymph nodes in the neck was in most cases the first sign noticed by the patient himself, and by which he might know that something was wrong — though it did not in all cases lead him to consult a physician. Such a swelling in the neck was in 30 of our 77 cases (40 per cent) the first symptom noticed by the patient. In most cases it did not cause any pain, and only 21 of the 30 went to doctor on its account, and then as a rule because it grew larger. The other 9 did not seek medical advice until later, when one or several other symptoms

had appeared, such as headache, impaired hearing, diplopia, nasal obstruction with secretion and epistaxis, and the like.

The lymph node swelling most often found in a patient suffering from nasopharyngeal tumor, — and which should suggest examination of the nasopharyngeal cavity; if necessary with biopsy, unless it is preferred to take the tissue sample from the node itself, — is situated posterior and inferior to the mastoid process; in other words in, or just below, the retromandibular fossa. In the early stages it is situated deeply and can only with difficulty be palpated, as it lies partly or wholly under the sternocleidomastoid muscle. It may in rather short time attain a considerable size. Curiously enough, several patients state that the size of these nodes may change somewhat. The lymph node tumescence is, as a rule, not of as firm consistence as the carcinoma metastases from cancer of the hypopharynx, but more elastic. The surface is comparatively smooth and even; periadenitic phenomena, if any, are little pronounced, so that even large lymph nodes are not fixed but mobile; there are no phenomena of softening; the skin over them is natural-looking and displaceable, and as a rule the nodes are not tender to the touch. The lymph node involvement associated with tumors of the nasopharynx is not infrequently bilateral, and in several cases a greater or lesser number of the deep-lying superior cervical lymph nodes, either in one side or in both, are involved; sometimes even the supraclavicular nodes.

The frequency of lymph node metastases from tumors of the nasopharynx is well illustrated by the fact that in 67 of our 77 cases (87 per cent) such metastases either were present when the patient was referred to us or developed sooner or later afterwards; while only in 10 no swollen lymph nodes could at any time be demonstrated with certainty.

As said, the *direct symptoms from the nasopharynx* are often overshadowed by those mentioned above, but of course they occur to a not inconsiderable extent. They consist in nasal obstruction, difficult respiration through the nose, nasal speech, secretion from the nose and epistaxis; more rarely difficulty of deglutition. In our material, these symptoms were in 26 cases the first signs of the disease, in 20 what led the patient to consult a physician. In these cases, the tumors have evidently been more or less voluminous, exophytic, filling a considerable part of the nasopharynx.

In some cases, *ankylosis of the jaw* may occur as the result of invasion into the pterygoid muscle; sometimes even as an early symptom, which misleads the diagnosis by suggesting trouble from the wisdom-tooth and makes mirror examination of the nasopharynx difficult.

During the further course of the disease, the lymph node metastases and the intracranial brain symptoms usually dominate the picture. In 25 cases, development of *distant metastases* was demonstrated with cer-

tainty either roentgenologically or at necropsy (*necropsy reports* exist in regard to 15 cases, in all). In 9 of these cases, the primary tumor in the nasopharynx had as a result of the irradiation treatment disappeared entirely by the time when the distant metastases manifested themselves. In 12 cases there were metastases to bones; in 8 of them at least to lumbar vertebrae. Besides, metastases were demonstrated in the mediastinum and lungs (8 cases), the liver (3 cases) and the abdominal glands (7 cases).

The variability, both in the initial stages and in the later course, was considerable. The patients whom the irradiation therapy failed to relieve of their symptoms died after greatly varying periods, in most cases owing to intracranial progression of the tumor, most often in cachexia, and in half of the cases with distant metastases. The average survival time for the 51 patients who have died up to the present was about 18 months counting from the day they were referred to us, a little over 2 years counting from the appearance of the first symptom. The length of their survival was undoubtedly in a great measure due to the roentgenologic treatment received.

Microscopic Anatomy

It is not yet quite clear how the malignant tumors of the nasopharynx should be classified histologically. Radiotherapeutic observations seem to indicate that most of them must be considered as immature neoplastic growths exhibiting marked radiosensitivity, but it has proved difficult to determine their histogenesis and rubricate them according to it.

Careful revision of our material, by Dr. Fridtjof Bang, histopathologist to the Radium Center, has led to the following classification: 22 (30 per cent) were lymphoepitheliomas, 13 reticulosarcomas (of which 2 plasmocytomas), 7 lymphosarcomas, 12 basal-cell carcinomas, 20 squamocellular carcinomas (of which 9 were parakeratosic) and only 1 a cylindrocellular carcinoma. Of 2 cases there was, as said, no microscopic examination.

If we consider the lymphoepitheliomas as reticulosarcomas, it will be seen that 35 (47 per cent) of our cases were of the latter type and that 42 (56 per cent) have been radiosensitive sarcomas, while of 33 carcinomas (44 per cent) only 21 (27 per cent) were differentiated forms. If we class the basal-cell carcinomas, which in our material have exhibited the same marked radiosensitivity as the sarcomatous tumors, with the group of immature, radiosensitive tumors, the latter comprises nearly three-fourths (72 per cent) of the whole material.

Diagnosis

The variegated clinical picture presents many difficulties for the diagnosis. As it will be clear from what has been said above, and as pointed out also by ZUPPINGER, among others, different types of syndromes in nasopharyngeal tumors may be distinguished: *respiratory* (pharyngeal), *auricular* and *metastatic* (in which the clinical picture is dominated by symptoms respectively from the pharynx, the ear and from lymph node metastases), *neurologic* (cerebral) and *ocular* (where symptoms from the base of the skull and the eye are dominating); and to these may perhaps be added a *dental* type, where the symptoms seem to point to the wisdom-tooth (ankylosis of the jaw).

Demonstration of the primary tumor in the nasopharynx and biopsy from there, are determining for the diagnosis. The radiotherapeutist must master both the indirect nasopharyngoscopy by means of mirror examination of the nasopharyngeal cavity and the direct endoscopic examination by introduction of some type of rhinoscope or other through the nasal fossa after anesthetisation of the nasal mucosa; which is of particlar value in the case of lockjaw.

Valuable supplementary information is obtained by roentgen examination of the nasopharynx and the base of the skull. Lateral roentgenologic films taken with a view to visualising the soft tissues as a rule give a good expression for the extent of the tumor; only in the rare cases where the growth of the latter was entirely submucosal, along one of the lateral walls of the nasopharynx, did we gain anything by radiographing the nasopharynx on pendant head after injection of contrast substance through the nose as recommended by ZUPPINGER. The roentgen examination of the base of the skull in half-axial projection is, as already said, an indispensable help to disclose bone destruction. Since eye- and cranial symptoms are so frequent in nasopharyngeal tumors, special ophthalmologic and neurologic examinations of the patient are recommended, such as were made in all our cases.

Localisation and character of lymphomas in the neck should make one think of examining the nasopharynx, but biopsy of lymph nodes in the neck should not be refrained from if the diagnosis cannot be established in other ways. The risk of the tumor spreading is probably by no means as great as generally supposed, especially if care is taken to have the microscopic examination made as soon as possible and to get the irradiation treatment instituted at once. In the presence of lymphomas in the neck one should, as a matter of fact, never leave it at the likely diagnosis of simple inflammatory adenitis and seek the starting point of the latter in the teeth, the oral cavity and the tonsils, but should

Fig. 4.

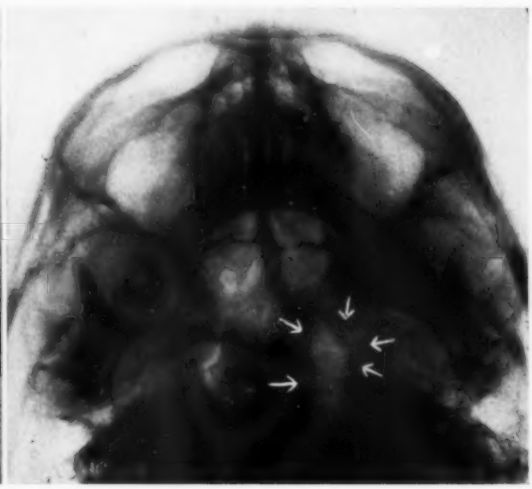

Fig. 5.

Fig. 4. — Roentgenogram of a large tumor in the nasopharynx, which fills the latter completely and displaces the soft palate downwards and forwards. Mirror examination could not be made, owing to ankylosis of the jaw.

Fig. 5. — Roentgenogram, in half-axial projection, of the base of the skull of a woman, aged 36 years. with lymphepithelioma of the nasopharynx, bone destruction in the left side, corresponding to the surroundings of the ~~jugular~~ foramen, with erosion of the apex of the petrous bone, the left side of the basioccipital bone and the posterior part of the body of the sphenoidal bone. (Case history no. 6)

always think of the possibility of a serious affection such as tuberculosis, leukemia, lymphogranulomatosis, lympho- or reticulosarcoma and, not least, metastasis from some not symptom-giving tumor in the upper air- and alimentary passages, — in the first place the nasopharynx. Here, the biopsy will settle the question. Aspiration biopsy by the ordinary method often fails in these cases, however. But not least in lymphomas of the neck we have for several years with good advantage used the biopsy trephine (described by CHRISTIANSEN in the Acta Radiologica XXI, 349, 1940), a small, sharp, motor-driven, rotating, hollow bore, by means of which a small column of tissue is drilled out for histologic examination. By this simple, rapid and only slightly injuring procedure we have nearly always succeeded in obtaining the histologic diagnosis, and we consider it as a valuable addition to the diagnostic armamentarium.

If the first biopsy from the nasopharynx or the lymph nodes in the neck is negative or not sure, one should not hesitate from one, or even

several, repetitions, if the clinical features of the case point to malignant tumor in the nasopharynx.

As it nowadays not infrequently is the case in tumor diagnosis, the finer diagnosis of malignant nasopharyngeal tumors thus as a rule requires the collaboration of several specialists: the rhinologist, the ophthalmologist, the neurologist, the radiologist and the histologist. Any one of these may become the one on whom the possibility and responsibility for the diagnosis first comes to rest; therefore both the diagnosis and the clinical picture of the nasopharyngeal tumors is of interest to all of them — as well as to the practising physician, who most often will be the one to whom the patient first comes with his complaint.

Table I

The first Symptom, and the Symptom which led the Patient to consult a Physician, in 77 Cases of nasopharyngeal Tumor.

	First symptom	Symptoms which led the patient to consult a physician
Lymph node tumor in the neck	30	21
Symptoms from nose and pharynx	26	20
» » middle ear	12	21
Trigeminus pain	8	11
Ocular symptoms (diplopia)	1	4
	77	77

Of great practical interest is the question of the *early diagnosis*, that is to say the first clinical symptom which may lead the patient to consult a physician and give the latter the possibility for establishing the diagnosis and institute the therapy without valuable time being lost. Table I shows the frequency of the different initial symptoms. It is not surprising to find that many of our patients had been under medical treatment for a considerable time under a wrong diagnosis before the true nature of the disease was recognised and an efficacious therapy instituted. On the average, over eight months elapsed, from the time when the patient observed the first symptom until treatment was begun; and the physician's part in this delay was nearly half of that time.

As it was found earlier by NEW in regard to a larger material, there are also among our cases many in which surgical operations, especially tonsillotomy and tonsilectomy, removal of nasal polyps, punctures and resections of the maxillary sinus, extractions of teeth and injections of alcohol into the trigeminus branches of the gasserian ganglion, had been done before they were referred to us; a striking evidence of the difficulty of the diagnosis in the early stages. There is little doubt, though, that

also in this respect advances will be made as familiarity with the symptomatology of the nasopharyngeal tumors becomes more widespread among specialists and practising physicians.

The roentgenologic Treatment

In the treatment of our patients, only fractioned irradiation with roentgen according to COUTARD's method has been used. Only slight modifications have been made in the therapy in the course of the years. The factors operated with have been 180—200 kv., 4—6 ma., as a rule strong filtration (Thoraeus filter), only in some few cases weaker filtration (0.5 Cu.); focus-to-skin distance 50—70 cm.; intensity, measured in air, 2.5—7.5 r/min. As a rule, two treatments daily were given, one in the forenoon, the other in the afternoon. The single dose has varied considerably, but has mostly been between 75 and 200 r (measured in air at the level of skin). It has depended in a great measure on the size of the field and the extent of the lymph node metastases; the patient's general condition and the local reactions having been very largely determining for the daily dosage. The greater part of the ray energy has been made to bear with frontal ray direction through two lateral fields, which at the same time included the lymph node metastases. In most cases, this was supplemented with irradiation of the primary nasopharyngeal tumor and the base of the skull through two smaller, anterior fields comprising the cheeks (the eyes being screened with lead), and with the central ray directed towards the opposite side at an angle of 45°, so that the two rays crosssed each other in the epipharynx. Through these two anterior fields, a not inconsiderable ray dose can be given to the nasopharyngeal tumor without charging the lateral fields too heavily. Fields over the forehead and the top of the head have been used only exceptionally. Occipital fields were tried in the beginning, but were soon given up, because the patients became ill with nausea and dizziness after irradiation through them. The size of the lateral fields have varied from 80 to about 150 cc., while the anterior fields have as a rule been under 50 cc. Where the lymph node metastases in the neck were so extensive that they included also the lower part of the latter, or perhaps the supraclavicular region, it was found of advantage not to make the field too large, but rather to irradiate the low metastases through an extra field; by this means it will as a rule be possible to avoid too strong general reactions.

It is important to have the upper limit of the lateral field situated high enough to ensure thorough irradiation also of the base of the skull, which always must be considered as a potential site for propa-

gation of the tumor. Since the lateral fields as a rule include both the parotid salivary glands, the irradiation generally causes a usually only temporary, but sometimes very discomforting diminution of the secretion of saliva, with dryness of the mucous membranes of the fauces and mouth, perversion and loss of taste. This reaction usually begins after one or two weeks' treatment and increases during the rest of the latter. The restoration of the parotid function depends on the dosage. With the dosage used by us, the dryness had generally become somewhat less pronounced a month or so after the end of the treatment, and thereafter slowly disappeared in the course of six months to a year. In most cases there is complete, or almost complete restitution of the salivary secretion and recovery of normal taste.

The total dose and the aggregate time of treatment has varied within wide limits. Only in the case of the few tumors where metastases could not be clinically demonstrated, could lateral fields be used of a size so relatively small that treatment with a sufficient tumor dosis could be carried through in fairly short time. The minimum of aggregate treatment time was 24 days, the maximum 72; the corresponding minima and maxima of total roentgen dosage to all fields 3,300 r and 10,000 r (measured in air).

The cutaneous reaction was in nearly all cases only a dry desquamation — epidermitis sicca; only in a few instances very slight, spotwise, superficial, moist epidermitis in the center of the fields. The limit to the tumor dose was not set by the tolerance of the skin, but by the general symptoms evoked in the form of anorexia, nausea and fatigue, due to the rather large fields and the resulting volume doses, which were necessary on account of the great extent of the lymph node metastases. Owing to the general condition of the patients, the treatment became, on the whole, a little more drawn out than desirable, but it was found necessary to go ahead cautiously according to the condition from day to day. In the mucosal linings of the nasopharynx and the tumor tissue in the latter, the irradiation produced in most cases only small, spotted patches, very rarely confluent false membranes.

It was always tried to carry the treatment through in one continous series, without interruptions. In cases of recurrence only a palliative effect was, as a rule, obtained by renewed treatment. In 2 cases, lasting freedom from symptoms was, however, obtained by repeated treatment, respectively for a residual tumor and a recurrence, 2 and 10 months after the first treatment.

The permanent alterations of the skin have been confined to partial epilation and slight teleangiectasia formation. In most of the cases there have been no pronounced permanent changes of the skin.

Result of the Treatment

The results obtained will be seen from Table II. Thirty-seven of the cases are from more than five years ago. Eleven of these (29 per cent) survived for over five years. Two of these 11 (5 per cent) were not symptom-free and have since died. One of these (a lymphepithelioma) was symptom-free for 3 years, then again developed metastases in the lymph nodes of the neck, which regressed after irradiation, and 2 years later a recurrence in the base of the skull, and died 8 years after the first treatment. The other (also a lymphepithelioma) was symptom-free for 2 years, then again got lymph node metastases in the neck, later recurrence in the nasal cavity and the base of the skull, and died 7 years after the treatment.

Table II

Roentgenologic Results in 37 Cases of nasopharyngeal Tumor 1931—1936.

Symptom-free after 5 years	9	(24 per cent)
Alive with recurrence after 5 years	2	(5 » »)
Died within 5 years	26	(71 » »)
	37	

Nine patients (24 per cent) passed the 5-year limit free from symptoms. One of these has since died of recurrence in the base of the skull and lymph node metastases $7^1/_2$ years after the treatment; the other 8 are alive and symptom-free respectively 11, 11, 10, 9, 8, 8, 7 and 7 years after the treatment. Three of them have thus passed the 10-year term. The histories of these 9 cases are briefly as follows.

Case 1. — Man, aged 40 years, referred to the Radium Center June 3rd, 1931. — For 18 months increasing deafness on right ear; insufflation without effect; in the last 3 months increasing nasal stenosis.

Objectively: Posterior rhinoscopy shows a flat ulceration in the roof of the epipharynx, extending over on the ostium of the tube and the posterior wall. *Biopsy: basal cell carcinoma.* — No lymph nodes, no roentgenologically demonstrable destructions of the base of the skull, no neurologic or ocular symptoms. — *Fractioned irradiation I:* Total dose 3,450 r_a (= 4,200 r_s)[1] in 23 (26) days; tumor dose 1,900 r. As a remnant of tumor persisted, *fractioned irradiation II* was given 2 months later: Total dose 4,250 r_a in 20 (24) days; tumor dose, 2,400 r. At the end of the treatment, the residual tumor had disappeared, a month later the patient's hearing was normal. He has since been controlled several times, last time 11 years after the treatment, is still symptom-free and attends to his work as civil engineer.

Case 2. — Man, aged 39 years, referred to the Radium Center June 25th, 1931. For over 6 months coryza, in the last two months singing in the right ear, for which in-

[1] r_a = roentgen measured in air; r_s = roentgen unit measured on the surface of the skin, including back-scatter.

sufflation has been given a couple of times. In the last month increasing attacks of pain in right cheek and temple, in the last two weeks slight ankylosis of the jaw. Consulted a physician two months ago.

Objectively: speech snuffling, slight ankylosis of the jaw, right side of soft palate slightly bulging. Posterior rhinoscopy shows a tumor as large as a pigeon's egg in the right side of the epipharynx. *Biopsy: lymphosarcoma.* — At right angle of the mandible a lymph node conglomerate the size of a date, at left angle a couple of hazelnut-sized nodes. No roentgenologically demonstrable destructions of the base of the skull; no neurologic or ocular symptoms. — *Fractioned irradiation:* Total dose 3,900 r_a (= 4,700 r_s) in 26 (42) days; tumor dose, 2,200 r. At the end of the treatment, the tumor had regressed, 6 weeks later also the lymph nodes. The patient has remained symptom-free since (11 years) with full capacity for work.

Case 3. — Man, aged 48 years, referred to the Radium Center Nov. 20th, 1931. For several years nasal stenosis and secretion, in the last months also deafness and epistaxis.

Objectively: Posterior rhinoscopy shows in the right side of the roof of the nasopharynx a lumpy tumor, larger than a hazelnut, which covers the right choana, involves the lateral wall and entirely covers the corner with the tube. *Biopsy: lymphepithelioma.* — No lymph nodes in the neck; no roentgenologically demonstrable destruction of the base of the skull; no neurologic or ocular symptoms. *Fractioned irradiation:* Total dose 6,000 r_a (= 7,200 r_s) in 23 (26) days. At the end of the treatment, the tumor had disappeared completely. The patient has since been controlled many times; he is still alive, and there are no signs of recurrence 10 years after the treatment.

Case 4. — Man, aged 59 years, referred to the Radium Center Jan. 7th, 1933. Nine months before, he had consulted an ear-specialist for pain in the left ear, had been »sufflated» and had had some »polyps» in the nose removed. Two months ago his hearing had diminished, there was nasal stenosis, and he had again had polyps in the nose removed.

Objectively: Left half of soft palate bulging. Posterior, rhinoscopy shows a walnut sized tumor, arising from the left side and filling the greater part of the epipharynx. *Biopsy: dictiocytic reticulosarcoma with plasma cells.* — No lymph nodes in the neck; no roentgenologically demonstrable destructions of the base of the skull; no neurologic or ocular symptoms. *Fractioned irradiation:* Total dose 3,375 r_a (= 4,050 r_s) in 25 (29) days; tumor dose, about 1,800 r. At the end of the treatment, the tumor had regressed; the patient has since been symptom-free for 9 years.

Case 5. — Young man, aged 16 years. referred to the Radium Center Nov. 7th. 1933. Four months previously, a circumscribed swelling had arisen upwards in the right side of his neck. Three weeks before he was referred to us, it had grown to the size of a hen's egg and had been excised. *Microscopy: lymphepithelioma.* In the last two months he had attacks of pain in the right trigemini I and II, and his hearing on the right ear had become reduced.

Objectively: Posterior rhinoscopy shows a large ulcerated tumor in the right side, covering the orifice of the tube. — In the retromandibular region and the superior carotid triangle there is a walnut-sized conglomerate of lymph nodes, and behind this a fresh, infiltrated cicatrix from an operation. Roentgen examination of the case of the skull shows a walnut-sized destruction in the right side of the latter, involving the pterygoid process, the ~~jugular~~ and oval foramens and the medial wall of the foramen spinosum. The right tympanon is retracted and redly transparent. There is slight hyperalgesia in the

region of the right trigemini I and II. — *Fractioned irradiation I:* Total dose 8,700 r_s in the course of 27 (34) days, tumor dose 4,000 r. Regression of primary tumor and nodes, but 10 months later a recurrence in the right side of the epipharynx was found, wherefore *fractioned irradiation II* was given: Total dose 7,500 r_s in the course of 27 (34) days; tumor dose, 3,550 r. In connexion with the treatment, suppurating otitis media in the right ear and mastoiditis developed, which were treated by paracentesis and resection of the mastoid process. The patient is now, 8 years after the treatment, without signs of recurrence and does his full share of work as farmer.

Case 6. — Woman, aged 38 years, referred to the Radium Center Dec. 23rd. 1933. A year before she was referred to us, she had, in connexion with a cold, got some swollen glands in the left side of the neck; which had since been steadily growing. Nine months before she came to us her deglutition became a little difficult, for which she was referred to an otolaryngologic service, where a polyp in the larynx was removed. In the following time she was given all-over carbon-arc light baths and 4 light, anti-inflammatory irradiations of the lymph nodes, and repeated punctures were done. Not until a week before she was referred to us was an excision from the lymph nodes in the neck, for biopsy, finally done. The microscopy showed *lymphepithelioma.*

Objectively: Posterior rhinoscopy shows upwards in the left lateral wall an ulcerated, flat tumor, which extends up into the roof and into the left posterior choana. — Upwards in the left side of the neck, under the sternocleidomastoid muscle, there is a lymph node conglomerate, fully the size of a hen's egg. — Roentgen examination of the base of the skull shows a soft-tissue shadow in the left half of the epipharynx; the left sphenoidal sinus is blurred and its posterior limits effaced. There is distinct destruction of the ~~jugular~~ foramen, involving the apex of the petrous portion of the temporal bone. —Neurologic examination shows paralysis of the left half of the soft palate and the accessory nerve in the left side. — Marked Horner's syndrome in the left eye. — *Fractioned irradiation:* Total dose 8,100 r_a (= 9,700 r_s) in the course of 48 (50) days; tumor dose, 4,700 r. The primary tumor and the lymph nodes in the neck regress completely. Roentgen examination of the base of the skull shows an almond-sized, sharply circumscribed, osseous defect around the ~~jugular~~ foramen, involving the apex of the pyramid. The paralysis of the left half of the soft palate and the left accessory nerve, as well as Horner's syndrome in the left eye, persist. After being perfectly well for 6 years, the patient develops symptoms from the base of the skull, and some time later lymph node metastases in the neck. Seven and a half year after the treatment she dies in another hospital, of tumor invasion in the case of the skull.

Case 7. — Woman, aged 34 years, referred to the Radium Center Feb. 1st, 1934. For 10 months previously treated as out-patient with all-over light baths and anti-inflammatory irradiations for lymph nodes in the left side of the neck.

Objectively: In the fauces, in the left lateral wall of the mesopharynx, just behind the left posterior palatine arch, a tumor-like, not ulcerated swelling, about the size of an unshelled almond; which at posterior rhinoscopy is seen to continue all the way up into the roof of the nasopharynx. *Biopsy: basal cell carcinoma.* Upwards in both sides of the neck, lymph node conglomerates about the size of a hen's egg, extending downwards to two fingers' breadth above the clavicle. No roentgenologically demonstrable destruction of the base of the skull; no neurologic or ocular symptoms. — *Fractioned irradiation I:* Total dose 9,360 r_a (= 11,200 r_s) in 47 (65) days; tumor dose, 5,400 r. At the end of the treatment, both the primary tumor and the lymph nodes have disappeared completely. — Three months later, a lymph node, the size of a large hazel-nut, is demonstrated in the left supra-clavicular fossa (just below the roentgenologic field).

It is treated with *fractioned irradiation II:* total dose 3,940 r_a (= 4,620 r_s) in 16 (18) days; tumor dose, 4,400 r. A superficial, moist epidermitis develops. The node regresses completely. Until now, 8 years after the treatment, there have been no further signs of recurrence or metastases.

Case 8. — Man, aged 50 years, referred to the Radium Center Dec. 15th. 1934. For 18 months increasing nasal stenosis and reduced hearing on the left ear. The speech somewhat snuffling.

Objectively: Posterior rhinoscopy shows in the nasopharynx a superficially ulcerated tumor filling the latter almost completely and extending beyond the corner of the tube on both sides. *Biopsy: lymphepithelioma.* — Under the upper end of the sternocleidomastoid muscle on both sides, a lymph node the size of a large unshelled almond. No roentgenologically demonstrable destructions of the base of the skull; no neurologic or ocular symptoms. — *Fractioned irradiation:* Total dose 8,030 r_a (= 9,600 r_s) in 36 (45) days. — At the end of the treatment, both the primary tumor and the lymph nodes have disappeared completely. The patient is alive, symptom-free and fully capable of work 7 years after the treatment.

Case 9. — Woman, aged 43 years, referred to the Radium Center July 2nd, 1935. Had a cold 3 months previously, with obstruction of the nose, which has persisted since.

Objectively: Posterior rhinoscopy shows in the nasopharynx a large, lobular, ulcerating tumor, arising from the right side of the posterior wall. *Biopsy: reticular sarcoma, partly syncytial.* — No lymph nodes in the neck; no roentgenologically demonstrable destructions in the base of the skull; no neurologic or ocular symptoms. — *Fractioned irradiation:* Total dose 6,340 r_a (= 7,600 r_s) in 42 (49) days; tumor dose, 3,600 r. At the end of the treatment, the tumor has disappeared completely. The patient has since been symptom-free for 7 years.

As it might be expected, an analysis of our material shows that the prognosis in the individual case depends on several factors; first of all on the histologic structure of the tumor, but also on its local extension, especially the involvement of the base of the skull, the size and extent of the lymph node metastases and the patient's general condition.

As it appears from the case histories given above, the tumor in 4 of the nine cases that remained symptom-free for five years had evidently not spread beyond the nasopharynx at the time when the treatment was instituted. The clinical symptoms in the anamnesis of these uncomplicated cases are chiefly pharyngeal (respiratory), as a rule accompanied by occlusion of the tube. The growth of these tumors has no doubt been more exophytic than infiltrative.

That long freedom from symptoms could also be obtained in spite of various complications and lymphogenic metastasising, is seen from the other five case histories. Lymph node metastases were present in them all, in two of them bilateral. In two cases, bone destructions in the base of the skull were demonstrated roentgenologically; in these there were neurologic symptoms, in one case referable to the 9th and 11th carvical nerves and Horner's syndrome, in the other to trigeminus I and II.

In none of the lastingly symptom-free cases were there any ocular symptoms (apart from Horner's syndrome), but other cases in our material, in which freedom from local symptoms was obtained but the patient died later of distant metastases, show that paralysis of the abducent nerve could often be cured completely.

To what extent the roentgenologic prognosis is governed by the histologic structure of the tumor will appear from Table III. Of the patients with sarcomatous tumors, 28 per cent remained symptom-free for over 5 years, of those with carcinomas 18 per cent. Of the 27 with the radiosensitive tumors (sarcomas and basal cell carcinomas), 9 (33 per cent) had over 5 years' freedom from symptoms; whereas none of the 9 with the more differentiated squamocellular carcinomas reached that limit.

Table III

Five-year Results of roentgenologic Treatment in 37 cases, in Relation to the histologic Type of the nasopharyngeal Tumor.

Lymphepithelioma	4 of 15	Sarcomas: 7 of 25 (28 per cent)
Reticulosarcoma	2 of 7	
Lymphosarcoma	1 of 3	
Basal Cell Carcinoma	2 of 2	Carcinomas: 2 of 11 (18 per cent)
Squamoepithelial Carcinoma	0 of 9	
No Microscopy	0 of 1	

The not altogether unfavorable results of the fractioned irradiation treatment of the malignant tumors in the nasopharynx are evidently due first and foremost to the fact that most of the tumors in that site are highly radiosensitive. From the anatomical point of view the conditions for the treatment, are, on the other hand, less favorable than with the other tumors in the fauces and pharynx, owing to the deeper situation and the extensive metastases.

A closer analysis of the individual cases shows that the failure of the treatment is probably in most cases due to considerable intracranial invasion, large, extensive, sometimes bilateral lymph node metastases, distant metastases and poor general condition of the patient. Only in a few of the cases, and only where it has been a case of more highly differentiated carcinomas, does it seem that the doses used have not been cancericidal in their effect on the primary growth in the nasopharynx. If better results are to be obtained in cases of this group, the dosage must be increased. This can be done in one of two ways; either by increasing the external roentgen dose (in which case smaller fields must be used, in order to make it possible to carry the treatment through), or by supplementary local irradiation with radium in the nasopharynx,

such as recommended by several authors. A condition for obtaining any advantage from such a supplementary irradiation, is however, that metastasising has not yet taken place or is, at least, very little extensive; and that there is no very deep invasion into, or through the base of the skull, what unfortunately only rarely will be the case. There is thus no reason to expect that material benefits will be derived from supplementary, intracavitary radium treatment, but it may perhaps be of service where the case is of the more highly differentiated squamocellular carcinomas.

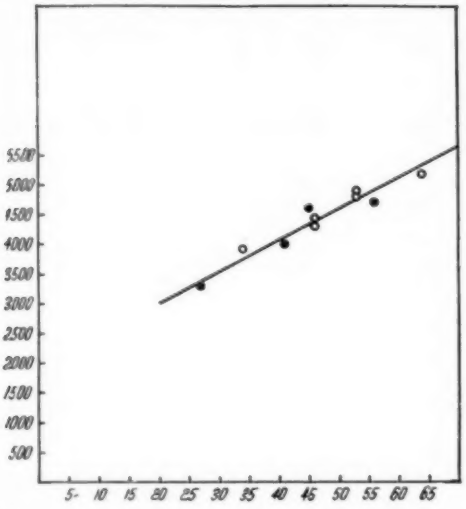

Fig. 6. — Tumor dose and total treatment time in 10 locally symptom-free cases of lymphepithelioma of the nasopharynx. — *The abscissa:* Treatment time (days); *the ordinate:* Tumor dose in units of r. Black dots: lastingly symptom-free cases; rings: locally symptom-free cases, later metastases.

There is more reason for expecting advantages from a better distribution in time, of the total roentgen dose, as pointed out by COUTARD. But to find a clinical basis for the best distribution is not easy. If we try from our results to arrive at a conclusion with regard to the dosage, and particularly with regard to its best distribution in time, one of the greatest difficulties is that we must count with different radiosensitivity of the different types of tumor. If we look at the relationship of dosage (calculated as dose in the tumor) to treatment time in our 9 symptom-free cases, we find a rather considerable variation. But if we take only those cases of lymphepithelioma in which there was lasting or local regression of the tumor, but which later recurred in the form of distant metastases or lymph node metastases lower down in the neck, outside the roentgenologic fields, we find that they group themselves in a coordinate-system of total doses and treatment times in such a manner that it seems that a line may be plotted for the ratio of dose to treatment time; which thus becomes an expression for the effect of the time factor (Fig. 6). On account of the small figures and other elements of uncertainty, this curve must be judged with some reservation, still, it may serve as expression for how high a tumor dose it is necessary, or desirable, to obtain within a given treat-

ment time in lymphepitheliomas of the nasopharynx, and thus also for the magnitude of the single and daily doses.

It seems as if the necessary tumor dose is about 3,000 r in the course of 20 days, 3,600 r in the course of 30, 3,900 r in the course of 40, 4,500 r in the course of 50 and 5,100 r in the course of 60 days. If we take the time factor for 20 days to be = 1, it will be for 30 days = 1.2, for 40 days = 1.3, for 50 days = 1.5, for 60 days = 1.7. As the tumor dose may grossly be estimated to be a little less than 50 per cent of the surface dose, the corresponding surface doses for 20, 30, 40, 50 and 60 days will be respectively 6,500, 7,500, 8,500, 9,500 and 10,600 r, that is to say that the daily dose for an aggregate treatment time of 3, 4, 5, 6, 7, and 9 weeks should be respectively 2×175, 2×150, 2×130, 2×120, 2×110 and 2×100 r.

It seems that it should be possible, by applying the method here outlined to a sufficiently large material, to find a basis for the variations of the time factor for the different types and localizations of malignant tumor, and thus to get a guide for the practical dosage. When sufficiently many clinically symptom-free cases shall have been collected, it will perhaps also become possible to find a particularly favorable ratio between tumor dose and treatment time, about which the symptom-free cases group themselves closely. Clinical observations, which cannot, however, be substantiated by figures, seem to indicate that with a treatment of less than 3 or over 6—7 weeks the results are poorer than those obtained with a treatment time within those limits. There also seems to be basis for believing that the more highly differentiated and radioresistant the tumor, the shorter treatment time and higher daily doses are required. Only with less differentiated, radiosensitive tumors can a long treatment time be used, and yet freedom from symptoms be obtained.

Though the best that can be done at present is probably, as recommended by COUTARD, to treat each case individually under constant surveillance of the tumor's regression and the local and general reactions to the irradiation, the figures given above may perhaps, despite all the elements of uncertainty in their calculation, with regard to one single field serve as guidance in the — on account of its empiricism — by no means easy task which fractioned roentgen irradiation of malignant tumors still is to-day.

If we compare the results obtained by us (Table II and III) with the results of radiologic therapy hitherto reported, we are immediately confronted with the difficulties arising from different and varying histologic classification. BERVEN (1926) obtained over 5 years' freedom from symptoms in 5 of 33 cases of carcinoma and 3 of 37 cases of sarcoma, by a combination of external irradiation (chiefly teleradium) and local

radium in the nasopharynx; COUTARD (according to CUTLER and DEL REGATO) obtained, chiefly by roentgen therapy alone, 5 years' freedom from symptoms in 7 cases out of 37 (lymphosarcomas, 5 of 22; lymphepitheliomas, 1 of 7; carcinomas, 1 of 9). SCHINZ & ZUPPINGER register: 5 years' freedom from symptoms, 0 of 5, 3 years freedom from symptoms 4 of 6, but do not give the histologic diagnosis of the individual cases.

The number of published cases of nasopharyngeal tumors that have been cured by radiation therapy is still small, but will no doubt increase considerably in the coming years.

SUMMARY

On the basis of 77 observations, in the years 1931—1941, at the Radium Center in Copenhagen, the author describes the polymorphous symptomatology of the malignant nasopharyngeal tumors, with emphasis on those symptoms that are of special importance for the diagnosis. The histopathology of the tumors is briefly discussed. The fractioned roentgen irradiation used, and the reactions produced by it, are described. The results of the treatment are presented and analysed, especially as regards the histologic picture. Of 37 cases, 9 (24 per cent) are symptom-free after five years or more; namely, of 25 sarcomas 7 (28 per cent), of 11 carcinomas 2 (18 per cent). None of the more highly differentiated carcinomas have remained lastingly symptom-free. Also complicated cases with involvement of the base of the skull and symptoms from the cranial nerves may become symptom-free for a considerable length of time. In conclusion, the author discusses the possibilities for improving the results of the treatment by supplementary intracavitary radium treatment and a better distribution in time of the roentgen dose.

ZUSAMMENFASSUNG

An Hand von 77 Beobachtungen aus den Jahren 1931—1941 in der Radiumzentrale in Kopenhagen, beschreibt Verf. die vielgestaltige Symptomatologie der bösartigen Nasen-Rachentumoren, mit Betonung derjenigen Symptome, die für die Diagnose von besonderer Bedeutung sind. Die Histopathologie der Tumoren wird kurz besprochen. Die verwendete fraktionierte Röntgenbestrahlung und die durch dieselbe erzeugten Reaktionen werden kurz beschrieben. Die Ergebnisse der Behandlung werden vorgelegt und analysiert, besonders was das histologische Bild anbelangt. Von 37 Fällen waren 9 (24 %) nach fünf oder mehr Jahren symptomfrei, und zwar von 25 Sarkomen 7 Stück (28 %), von 11 Karzinomen 2 (18 %). Keines der höher differenzierten Karzinome blieb dauernd symptomfrei. Selbst komplizierte Fälle mit Befallensein der Schädelbasis und Kranialnervensymptomen können auf beträchtliche Zeit symptomfrei werden. An Hand dieser Befunde bespricht Verf. die Möglichkeiten, die Ergebnisse der Behandlung durch zusätzliche intrakavitäre Radiumtherapie und bessere zeitliche Verteilung der Röntgendosis zu verbessern.

RÉSUMÉ

Sur la base de 77 observations des années 1931 à 1941, provenant du Centre du Radium de Copenhague, l'auteur décrit la symptomatologie polymorphe des tumeurs malignes du nasopharynx, en insistant sur ceux des symptômes qui ont une importance

spéciale pour le diagnostic. Brève discussion de l'anatomie pathologique de ces tumeurs. Description de la méthode de radiothérapie fractionnée dont il est fait usage, ainsi que des réactions qu'elle provoque. Les résultats du traitement sont présentés et analysés, en tenant particulièrement compte de l'image histologique. Sur 37 cas, 9 (24 %) sont indemnes de tout symptôme pathologique après cinq ans et plus: à savoir, 7 des 25 sarcomes (28 %), et 2 des 11 carcinomes (18 %). Aucun des carcinomes à différentiation plus avancée n'est resté durablement guéri. Même des cas compliqués, avec envahissement de la base du crâne et symptômes du côté des nerfs craniens, peuvent être débarrassés de tout signe maladif pour un laps de temps considérable. En guise de conclusion, l'auteur discute de la possibilité d'améliorer les résultats thérapeutiques par l'adjonction supplémentaire d'un traitement intracavitaire par le radium et une meilleure répartition dans le temps de la dose de Rayons Roentgen.

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TRAVAIL DU CENTRE ANTI-CANCÉREUX DE ODENSE (DIRECTEUR: DOCTEUR PAUL JACOBY, MÉDECIN EN CHEF) ET DE L'INSTITUT PATHOLOGIQUE DE FIONIE (DIRECTEUR: JOHS. VESTERDAL JØRGENSEN)

NAEVOÉPITHÉLIOMA NON PIGMENTÉ À L'ÉVOLUTION LENTE PRÉSENTANT UNE IMAGE HISTOLOGIQUE PEU CARACTÉRISTIQUE[1]

par

Jens Munck Nordentoft

L'observation que voici, n'est pas rapportée à cause de sa rareté, mais elle nous paraît intéressante, soit par la lenteur d'évolution ne ressemblant guère à la marche habituelle des naevoépithéliomas, et pour le bon effet palliatif du traitement radiothérapique, soit, et surtout, en raison des difficultés que présentait le diagnostic, principalement le diagnostic microscopique.

Un ouvrier électricien, âgé de vingt-trois ans, toujours bien portant, vient en consultation, le 29 décembre 1936, au Centre anticancéreux de Odense, pour une marque de naissance au front, qu'il avait toujours eue. Quatre ou cinq mois avant la consultation, il l'avait taquinée, puis une petite tumeur s'était développée. Celle-ci se présentait maintenant comme une tumeur rouge bleuâtre, pédonculée, du volume d'un pois. L'affection est considérée comme un *granuloma téléangiectaticum*, et est enlevée par électrocoagulation. Lors d'un examen, fait trois mois plus tard, aucune trace ne restait.

En automne 1937, le malade constate la présence, devant l'oreille gauche d'un néoplasme de la grosseur d'un pois. Cette tumeur augmente jusqu'à atteindre, au cours d'une année, la dimension d'une noix. Comme, un soir, le malade ressent subitement un endolorissement assez prononcé derrière l'oreille, accompagné de tuméfaction et de pulsation, il est admis, le lendemain, 6 septembre 1938, au service chirurgical de l'Hôpital militaire de Copenhague. L'examen pratiqué ici décèle, devant l'oreille gauche, une partie de 5 sur 3 cm, douloureuse et indurée, et derrière cette oreille et la branche du maxillaire inférieur une petite bosse endolorie. Sécrétion abondante de la salive. A part cela, l'examen ne montre rien d'anormal. Le sondage du canal de Sténon et la radiographie pratiquée en plusieurs projections n'ont pas révélé des signes de calcul salivaire. Une semaine après l'hospitalisation l'intumescence a un peu diminué de volume, elle est maintenant de la grosseur d'une cerise, palpable au dehors de la parotide comme une tumeur assez isolée, rappelant soit une adénite soit une loupe. — Le lendemain, 14

[1] Remis à la Réd. le 26 Sept. 1944.

septembre, on pratique une *excochléatio:* L'intumescence, située immédiatement derrière la parotide, contient et du pus et quelque chose ressemblant à une membrane d'abscès, ce qui nous porte à croire, qu'il s'agit d'une loupe infiltrée, éventuellement d'un tératome.

Examen histologique du fragment prélevé (H. Seemann, 17 septembre 1938):

Le tissu, qui est en plusieurs petits fragments, se compose essentiellement de masses cellulaires formées de cellules assez polymorphes, pour la plupart à tendance fusiforme. Les cellules ne produisent pas directement de fibrilles conjonctives, cependant, entre les masses cellulaires, on trouve de larges traînées de tissu conjonctif. Certains endroits du tissu présentent un aspect nécrotique, tandis qu'ailleurs on peut observer du tissu conjonctif en train de se constituer et de l'infiltration leucocytaire. Dans une partie de la préparation, les cellules fusiformes signalées plus haut sont groupées, par rapport au tissu conjonctif, d'une manière qui rappelle la prolifération endothéliale dans un ganglion lymphatique. Aucun signe de tuberculose. D'après sa structure, on doit regarder le tissu comme du tissu tumoral, probablement de structure sarcomateuse ou endothéliale.

Diagnostic microscopique: — *Sarcome fusocellulaire.*
— *Endothélio-sarcome?*

La préparation fut en outre soumise à l'examen d'un autre histologiste compétent. Celcui-ci était de l'avis qu'il s'agissait d'une tumeur mixte atypique de la parotide.

Le malade quitta le service le 30 septembre. La plaie s'était cicatricée sans complications.

Diagnostic du service: *Tumeur rétroparotidienne.*

L'intumescence augmentant toujours de volume, le malade est réadmis, le 17 octobre 1938, au service chirurgical de l'Hôpital militaire, où il reste jusqu'au 19 novembre 1938. A présent, on recourt à l'application d'un traitement radiothérapique. On donne 3,000 r à doses fractionnées (du 20 octobre—16 novembre 1938) réparties sur deux champs tangentiels. Filtre: $^1/_2$ mm Cu × 3 mm Al; distance anticathode-peau: 40 cm. (160 KV, 3 MA.).

Le 25 octobre, on procède à l'ablation chirurgicale de la cicatrice et d'une chéloïde grosse comme la moitié d'un pois.

5 mois plus tard le malade est de nouveau hospitalisé au Centre anticancéreux de Odense (14 avril—11 mai 1939), une tumeur glandulaire s'étant entre-temps développée sur le cou au-dessous de l'angle gauche du maxillaire inférieur. Cette tumeur était dure, grosse comme une noix. La tumeur devant l'oreille gauche était de consistance ferme, bien limitée, de la taille d'une noisette. On constate l'apparition, sur le front, du côté gauche, à l'endroit de l'affection antérieure, de deux petits nodules, l'un de la dimension d'une amande de noisette, dur, mobile sur l'os sous-jacent, l'autre du volume d'un pois à peine, fixé. Le malade s'était d'ailleurs senti en bonne santé. Pas de symptômes cérébraux, aucune gêne de la vision, aucun trouble de l'audition; il n'existe pas de difficultés de déglutition, aucuns symptômes du côté des voies respiratoires. L'examen clinique n'a rien décelé d'anormal, abstraction faite de ce que nous venons de signaler.

A présent, on regarde l'intumescence du front comme étant une métastase, et elle est prélevée pour l'examen patholo-anatomique.

Examen microscopique du fragment tissulaire prélevé au front (Kaj Røjel, le 20 avril 1939):

Le petit fragment de peau contient, à 5 mm environ de la surface, une tumeur arrondie, nettement limitée, grosse comme une tête d'épingle. Cette tumeur est constituée de cellules ressemblant aux cellules épithéliales et variant assez en taille et en forme.

D'une part, on voit des cellules assez petites et minces, à noyau en bâtonnet un peu foncé, d'autre part, on note des cellules plus grandes, à noyau plus clair, arrondi ou ovoïde, parfois boursouflé. Les limites cellulaires sont parfois nettes, mais le plus souvent elles sont assez peu distinctes. Enfin, on remarque des amoncellements de cellules à type lymfocytaire avec un protoplasma rare et à noyau sombre, arrondi, formant, entre les autres cellules, de petits amas plus ou moins circumscrits.

Les cellules tumorales, dans lesquelles on n'a pu constater des mitoses, sont groupées soit tout à fait irrégulièrement, soit dans de petites accumulations plus ou moins circumscrites, ou dans des traînées ou des colonnes assez longues qu'il sera possible, en montrant un peu de bonne volonté, d'interpréter comme du type cylindromateux.

En raison des renseignements rapportés plus haut, et parce qu'on ne saurait s'expliquer la tumeur d'aucune autre manière, on penchera à croire, qu'il s'agit d'un épithélioma métastatique.

Abstraction faite de la tumeur sus-décrite, le fragment de peau ne présente rien d'anormal.

Diagnostic microscopique: *Epithélioma métastatique.*

Un traitement radiothérapique du côté gauche du cou avait été commencé aussitôt. On a donné au total 1980 r par doses fractionnées, réparties sur deux champs. Filtre: $^1/_2$ mm Cu: distance anticathode-peau: 40 cm. Maintenant la radiothérapie de contact (»Monopan» 60 KV, 4 MA, Filtre environ 0,15 mm Cu) fut appliquée à l'affection frontale, au total 3,000 r à une distance anticathode-peau de 3 cm quatre irradiations de 750 r chacune sur un champ d'environ 2×2 cm. L'irradiation de contact a également été appliquée à la tumeur située devant l'oreille. Cinq fois 500 r. Distance anticathode-peau: 3 cm.

Les affections ont un peu diminué après les traitements par les rayons Roentgen, et pendant l'année suivante l'état du malade restait presque stationnaire, abstraction faite, toutefois, de l'apparition d'un ganglion supra-claviculaire, gros comme une noisette, traité en janvier/1940, aux rayons Roentgen (1920 r, filtrées par $^1/_2$ mm Cu à une distance anticathode-peau de 33 cm). Le ganglion a disparu après le traitement.

Au mois de mai 1940, nouveau traitement radiothérapique des ganglions devant l'oreille gauche (irradiation de contact, »Monopan», 4,000 r).

En juillet 1940 apparaît, dans l'aisselle gauche, un nodule de la taille d'une noix. Ce nodule est traité avec au total 2,400 r, filtrées par $^1/_2$ mm Cu à une distance anticathode-peau de 40 cm.

En février 1941 apparut une nouvelle intumescence dans la région temporale gauche, de sorte qu'on notait à présent des tumeurs juste au-dessus du sourcil gauche, devant la parotide et, enfin, près du bord de l'avant du muscle sternocleïdo-mastoïdien. Le ganglion supra-claviculaire n'était plus perceptible. Celui de l'aisselle gauche était plus petit qu'une noisette. Les altérations faisaient penser plutôt à des métastases cancéreuses qu'à un sarcome.

A présent, la radiographie pulmonaire permet de constater, correspondant au 4.e espace intercostal (compté à l'avant), deux ombres d'un diamètre de 12 et de 18 mm rappelant des métastases. Plusieurs radiographies pulmonaires faites antérieurement avaient été négatives.

Jusqu'ici l'état général n'était pas compromis. Cependant, en avril 1941, le malade se plaint de douleurs dans la région parotidienne, et de nouveaux nodules se développent: dans l'aisselle droite, dans le cuir chevelu, dans la moitié thoracique gauche. Les métastases pulmonaires ont également augmenté de volume.

(Traitement aux rayons Roentgen (19 avril—8 mai) de la joue gauche, des deux aisselles et du thorax).

Dans le courant de l'été, l'état général du malade décline. Il est fatigué, incapable de travailler, sans appétit. Il se plaint de vives douleurs au côté gauche de la tête et dans le fémur droit. De nombreuses métastases dures, mobiles sous la peau, atteignant jusqu'au volume d'un pois se développent sous la peau du tronc, des bras et des jambes; les unes sont indolores, les autres très douloureuses (en particulier celles de la cuisse droite et de l'aisselle droite). Quelques-unes sont traitées aux rayons Roentgen — plutôt solaminis causa; On donne en outre un traitement de radiothérapie générale.

L'examen radiographique, pratiqué au mois d'août, du bassin et du fémur droit était négatif. Les métastases pulmonaires avaient grandi, la plus grande jusqu'à mesurer presque 3 sur 3 cm.

Il apparaissait de petites tumeurs dures, mobiles, du côté gauche du scrotum au niveau du cordon spermatique. Le malade se plaignait beaucoup de fourmillements aux jambes, et des difficultés de déglutition s'installaient. (Pourtant, la radiographie de l'oesophage a montré des conditions normales). On donnait de fortes doses de scopolamine-morphine, et le malade fut soumis — solaminis causa — à une radiothérapie générale.

Au mois d'octobre, il se plaint de vision double en regardant vers la droite, et lors d'un examen fait par un oculiste, on note une parèse du muscle inférieur gauche. L'état général du malade baisse de plus en plus, et l'exitus se produit le 23 novembre 1941.

Autopsie:

Examen extérieur: Etat d'amaigrissement extrême et de cachexie. Partout dans la peau de nombreux nodules mobiles, du volume à partir d'un pois jusqu'à d'une cerise à peine. Une intumescence assez grande dans la région de l'angle gauche du maxillaire inférieur. Pas de cyanose ni d'oedèmes.

Poumons et plèvres: Les plèvres sont libres. Il n'y a pas d'exudat. Les poumons sont de volume moyen, rouge bleuâtres, à la surface lisse. Le lobe inférieur du poumon droit contient dans la partie centrale une masse tumorale presque des dimensions d'une pamplemousse, jaune blanchâtre, uniforme, assez molle, et bien limitée. La surface en est irrégulière et bosselée. Le tissu pulmonaire avoisinant est le siège d'une atélectasie de compression. Le reste du tissu pulmonaire est normal, plein d'air. Aucun signe de pneumonie ni de tuberculose. Les bronches et les ganglions du hile ne présentent rien d'anormal.

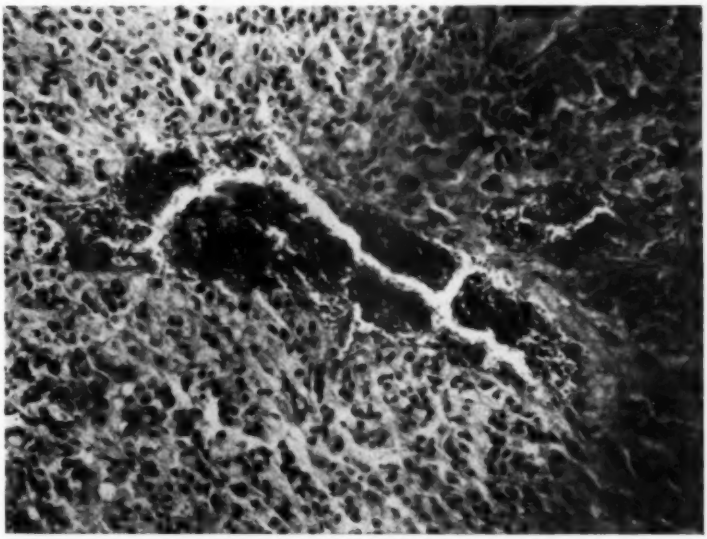
Coeur et péricarde: Le coeur, dont le volume est légèrement augmenté, doit cette augmentation à une dilatation modérée de toute la moitié droite du coeur. On trouve, dans l'oreillette droite et dans le myocarde du ventricule droit, près de la surface 3 ou 4 métastases tumorales jaunes blanchâtres, bien limitées, de consistance molle.

Vaisseaux, oesophage, estomac ne présentent rien de pathologique.

Canal intestinal: Une dizaine de métastases tumorales du volume d'un pois se trovent dispersées dans la paroi et de l'intestin grêle et du gros intestin. On en trouve également plusieurs dans la racine du mésentère et au long de l'insertion de celui-ci à l'intestin, de même que dans le grand épiploon. Pas d'ascite.

Pancréas ne présente rien de pathologique.

Capsules surrénales: La surrénale gauche à peu près de la taille d'un oeuf d'oie. La surface en est lisse, couverte d'adhérences fibreuses. A la coupe, on voit le tissu tumoral assez mou, d'un aspect bigarré. Dans le tissu pris en général, des parties rougeâtres alternent avec des parties blanches, cependant, çà et là, on trouve des taches jaune d'ocre, d'un diamètre d'environ 1 cm $^1/_2$. La surrénale droite est grosse comme un oeuf de canard, elle présente un aspect exactement identique à celui que nous venons d'écrire. Les tumeurs surrénales sont bien délimitées et n'envahissent pas les organes avoisinants.



Coupe d'une métastase surrénale. — On remarque le rapport intime des cellules avec la paroi vasculaire, prêtant à la tumeur une pointe endocrinienne qui contribuait à la première conception de la tumeur comme endothéliosarcome et tumeur de la surrénale. L'aspect tumoral est, en ce point-ci, en partie épithélial, cependant, en bas et à droite, on distingue un passage à des régions sarcomatoïdes.

Foie: Normal quant au volume et à la forme. Un peu au-dessous de la face capsulaire on remarque çà et là des métastases tumorales, pouvant atteindre jusqu'à la grosseur d'un pois. Le canal cholédoque paraît également engainé de tissu néoplastique, tandis que le passage biliaire à l'intestin est libre. On ne voit pas de dilatation.

Rate: La rate est hyperémique, le volume en est légèrement augmenté, la pulpe ferme.

Ganglions lymphatiques: Une partie des métastases tumorales palpables dans le mésentère et dans le grand épiploon et — peut-être — de celles dans la peau, sont, sans aucun doute, des métastases ganglionnaires.

Reins et voies urinaires ne présentent rien de pathologique.

Organes sexuels ne présentent rien de pathologiques.

Système nerveux central: On procède à l'ouverture du crâne. Les impressiones digitatae sont plus marquées qu'à l'ordinaire, et l'os est un peu aminci, pellucide. Les méninges sont normales. Le tissu cérébral est exceptionnellement ferme, phénomène dû probablement à un oedème prononcé. Les coupes habituelles sont pratiquées dans le cerveau, le cervelet, la protubérance, et la moelle allongée; on ne constate nulle part la présence de métastases tumorales ni de signes d'hémorrhagies ni de ramollissement. Pas d'abcès.

Diagnostic d'autopsie: — Tumeur glandulaire bilatérale maligne de la surrénale.
— Métastases multiples.
— Oedème cérébral.
— Légère dilatation du coeur.
— Cachexie.

Sont prélevés pour l'examen histologique:

1) La capsule surrénale gauche, 2) la capsule surrénale droite, 3) des nodules cutanés. 4) des métastases du grand épiploon.

Les coupes du tissu tumoral des deux surrénales présentent, en principe, un aspect identique: tissu tumoral à nécroses. On perçoit aux coupes examinées des champs microscopiques, où le tissu tumoral ressemble très étroitement à la cortico-surrénale en présentant, toutefois, quelque atypie et de l'inégalité cellulaire. La masse principale du tissu est formée d'assez grandes cellules claires, polygonales, à noyau arrondi ou ovale, quelquefois un peu anguleux. Çà et là, on discerne des cellules à noyaux multiples. Il y a parfois une certaine polymorphie et inégalité, mais ces anomalies sont loin d'atteindre le degré qu'on peut voir dans les tumeurs cortico-surrénaliennes. Le plus souvent le protoplasma est vide. A certains endroits la polymorphie est remplacée par un aspect plus uniforme; les cellules deviennent plus petites, plus minces, çà et là presque fusiformes et très homogènes, affectant ainsi une structure sarcomatoïde assez difficile à interpréter sans la transition insensible vers le reste du tissu tumoral.

Sur les coupes cutanées on trouve une tumeur assez bien limitée, constituée de tissu tumoral du type ci-dessus décrit. Il en est de même pour le tissu tumoral prélevé au grand épiploon.

L'hypothèse adoptée premièrement était qu'il s'agissait d'un épithélioma glandulaire bilatéral de la surrénale, et que les tumeurs cutanées traitées antérieurement en étaient des métastases.

Quelque temps après on reçut à l'Institut pathologique une préparation prélevée à un ganglion inguinal renfermant des métastases d'un naevus enlevé peu de temps avant. Il s'agissait d'un naevoépithélioma non pigmenté, qui, après argentation selon la méthode de da Fano, n'a pas même montré des phases initiales de mélanine. Pendant le travail avec ce cas, on s'est souvenu du cas qui nous occupe, et une revision avec des colorations spéciales a maintenant permis de constater que la tumeur, regardée primitivement comme une tumeur surrénalienne avec des métastases, était en réalité un naevoépithélioma dont les métastases aux surrénales, de par leur ressemblance avec du tissu surrénal avaient égaré l'histologiste.

Ce cas forme une très belle illustration de l'endroit dans le Précis de Pathologie de Boyd, où il dit: »Aucune tumeur ne présente un aspect plus varié que le mélanome, et il ne sera pas trop dire, qu'il puisse simuler épithélioma, sarcome, endothéliome, même lymphosarcome». On pourrait y ajouter, pour le cas qui nous occupe, tumeur mixte de la parotide, endothéliosarcome, tumeur corticosurrénale (voir microphotographie).

Résumé de l'histoire du cas rapporté:

Chez un jeune homme, âgé de vingt-trois ans, une tumeur, grosse comme un pois, s'est développée au front, après irritation d'un naevus. La tumeur, enlevée en 1936 par électrocoagulation, est regardée comme un *granulome*. L'examen microscopique n'a pas été pratiqué. Au bout

d'une année apparaît, devant l'oreille gauche, un néoplasme de la grosseur d'un pois, augmentant de volume pendant l'année suivante jusqu'à atteindre les dimensions d'une noix. L'étude macroscopique ne permet pas de déterminer la variété tumorale (*adenite?*, *loupe?*). L'examen microscopique aboutit au diagnostic: *sarcome fusocellulaire?*, *endothéliosarcome?*, *tumeur mixte de la parotide?* Le traitement par rayons Roentgen réduit la tumeur au volume d'une noisette. Six mois plus tard, une tumeur glandulaire s'est développée au côté gauche du cou, de même qu'on constate la réapparition de quelques nodules au front. La biopsie pratiquée sur ceux-ci donne le diagnostic microscopique: *épithélioma métastatique?* Ces tumeurs diminuent sensiblement après application de roentgenthérapie. Il en est de même pour un ganglion supraclaviculaire ainsi que pour un nodule dans l'aisselle gauche, apparu dans l'été de 1940, 3 ans et demi après le traitement de l'affection frontale. Peu à peu des métastases pulmonaires se développent, ainsi que de nombreuses métastases souscutanées, et le malade succombe sous l'image de cachexie plus de cinq ans après l'apparition de la tumeur initiale dans la peau du front.

Dans le service, on avait soupçonné la tumeur frontale d'être le foyer initial en supposant qu'il pouvait s'agir d'un naevoépithélioma.

A l'autopsie, l'étude macroscopique a décelé un grand néoplasme dans le lobe inférieur du pumon droit et de grandes tumeurs dans les deux surrénales ainsi que de nombreuses métastases assez petites ailleurs. A l'examen microscopique, on était d'abord porté à croire qu'il s'agissait d'un épithélioma bilatéral de la surrénale à métastases multiples. Ce n'est qu'après un nouvel examen fait avec des colorations spéciales qu'on a pu constater qu'il s'agissait d'un naevoépithélioma non pigmenté, dont les métastases aux surrénales ressemblaient au tissu surrénal.

L'observation, que nous venons de rapporter, se caractérise très bien par la citation ci-dessus alléguée du Précis de Pathologie de Boyd: »Aucune tumeur ne présente un aspect plus varié que le mélanome, et il ne sera pas trop dire, qu'il puisse simuler épithélioma, sarcome, endothéliome, même lymphosarcome». On pourrait y ajouter, comme nous venons de le faire, pour le cas qui nous occupe, tumeur mixte de la parotide, endothélio-sarcome, tumeur cortico-surrénalienne.

RÉSUMÉ

Un cas de naevoépithélioma non pigmenté à métastases multiples est rapporté. Un naevus dans la peau du front est regardé comme foyer initial. Au début, les métastases sont traitées par les rayons Roentgen avec un très bon effet palliatif, cependant au bout de cinq ans, le malade succombe.

Le diagnostic microscopique présente de grandes difficultés, en ce sens qu'à différents moments on propose entre autres choses qu'il puisse s'agir d'un sarcome, d'un épithélioma et de tumeur cortico-surrénalienne. Seulement des colorations spéciales des préparations provenant de l'autopsie permettent de constater qu'il s'agit d'un naevoépithélioma non pigmenté.

SUMMARY

Report of a case of non-pigmented nevoepithelioma with multiple metastases. A nevus of the skin of the forehead was assumed to be the primary focus. Roentgen treatment of the metastases had a favourable and palliative effect for a time, but at the end of 5 years the patient succumbed.

The microscopical diagnosis encountered great difficulty because of the findings having on different occasions and among other conditions also suggested the presence of sarcoma, epithelioma and cortico-suprarenoma.

Not until the post-mortem examination was made was it possible to establish the diagnosis of non-pigmented nevoepithelioma and then only with preparations stained in a special manner.

ZUSAMMENFASSUNG

Es wird über einen Fall von unpigmentiertem Nävoepitheliom mit multiplen Metastasen berichtet. Ein Nävus der Stirnhaut wird als Initialherd angesehen. Anfangs wurden die Metastasen mit ausgezeichnet palliativem Erfolg mit Röntgenstrahlen behandelt, doch ging der Kranke nach fünf Jahren zugrunde.

Die mikroskopische Differentialdiagnose bietet grosse Schwierigkeiten, so dass man zeitweise u. a. vermutete, es könne sich um ein Sarkom, um ein Epitheliom oder um einen Nebennierenrindentumor handeln. Erst Spezialfärbungen von bei der Sektion gewonnenem Material erlaubten die Feststellung, dass es sich um ein unpigmentiertes Nävoepitheliom handelte.

FROM THE RADIOLOGIC SERVICE OF THE STATE HOSPITAL, COPENHAGEN
(CHIEF: PROF. FLEMMING MØLLER, M. D.)

PERIODIC, SPONTANEOUSLY REMITTENT VOLVULUS AND THE SYMPTOMS IN CASES OF COLON ELONGATUM[1]

by

Flemming Nørgaard, M. D.

The picture immediately suggested to most by the term: volvulus is no doubt that of an acute ileus due to an intestinal loop's or packet's turning about its mesentery, from which results a more or less complete occlusion of the gut and at the same time circulatory disturbances in the portion of the intestine involved and in the mesentery. Many cases develop, however, under much less alarming, often intermittent symptoms; and it has also long been known that lesser turnings of intestinal loops — of up to 180 degrees — about their mesentery not infrequently occur without producing symptoms as those just named. As »volvulus» simply means: twisting, the term is applied also to these last-named cases, but with the qualifying adjectives physiologic, symptom-free, attached; to distinction from the first-named, which, according to this classification, are termed, pathologic, symptom-giving volvulus.

It is not, however, the extent of the mesenterial torsion, measured in degrees, which alone determines whether a volvulus gives rise to symptoms or not; though it is, of course, an important factor in that respect. Thus, a volvulus of 180 degrees not infrequently produces severe symptoms; while, as said, a great many other cases remain entirely symptom-free. Even cases of 360 degrees' volvulus have been described (HOLMGREN), which gave no symptoms at all, except obstipation.

Among the factors determining for the symptom-giving or symptom-free course must be mentioned the greater or lesser compression of the lumen of the intestine at the point of the torsion, which depends partly on the abdominal conditions in regard to space, partly on the tightness of the mesentery at the site of the twist, and also on the nature and quantity of the contents of the gut. Of equal importance is the condition of the circulation in the portions of the intestine and mesentery involved; which is influenced by precisely the same factors. Also the torsion of

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the intestine about its own longitudinal axis which always accompanies a twisting of the mesentery is often determining for the occurrence of the symptoms. This so-called axial torsion, which in degrees amounts to twice as much as the twist of the mesentery (GROTH), is primarily distributed evenly over the whole of the twisted loop, and sometimes also beyond this to adjoining portions of intestine with mesenterial attachment; and in that case it does not give rise to symptoms and is probably often not noticed at all. But secondarily it sometimes becomes pressed together to a short section of the gut, and when that is the case it often causes complete occlusion of the latter.[1]

When once attention is directed to the occurrence of slight changes in the situation of the colon, and particularly to the presence of axial torsions, which often are more conspicuous than the causative volvulus especially if the latter is in the small pelvis or is partly hidden by contrast-filled coils of intestine, such cases are not infrequently met with among those referred to the roentgenologist for intestinal examination, both from medical and surgical, stationary and policlinical services. In a number of these cases it is without doubt a matter of incidental finding of a »physiologic» volvulus which has not given rise to symptoms (Figs. 1, 2, 3, 4).

ad Fig. 1. — Woman, 30 years old. For many years sluggish bowels; therefore frequent resort to laxatives. Never any abdominal pains. At the routine clinical examination, positive benzidine reaction found in the feces; therefore roentgen examination, which showed an abnormally long sigmoid colon. After part of the contrast fluid had been quitted, a small volvulus of about 180° was seen, with two axial torsions, one to each side of the twist; but none of them hindered the passage of the enema.

ad Fig. 2 a—b. — Woman, 32 years old, formerly operated on for extrauterine pregnancy, now complaining of various abdominal troubles, but not presenting any actual intestinal symptoms. Roentgen examination showed an abnormally long sigmoid, and, after part of the contrast fluid had been quitted, distinct axial torsion at a point of the descending colon. This torsion shifted its place between two exposures. There was probably a volvulus of the sigmoid; but whether this was the case could not be determined with certainty, because the gut lay collapsed in the small pelvis.

ad Fig. 3. — Woman, 44 years old, with peptic ulcer of the jejunum after former gastroenteroanastomosis for gastric ulcer. Since childhood suffering from obstipation; for several years alternately hard and soft stools. Roentgen examination of the colon showed, after part of the contrast fluid had been quitted, a distinct axial torsion at the junction of the sigmoid and the descending colon.

ad Fig. 4. — Woman, 49 years old, with cancer of the pancreas. Stools loose, frequent diarrhea, but otherwise no intestinal symptoms. Roentgen examination showed an abnormally long sigmoid, which under injection of the contrast fluid presented a volvulus of 180 degrees, and at the junction of the rectum and the sigmoid a distinct axial torsion of about 180°.

[1] About the mechanism of the axial torsion see GROTH, 1934; LAURELL, 1937; NØRGAARD 1941.

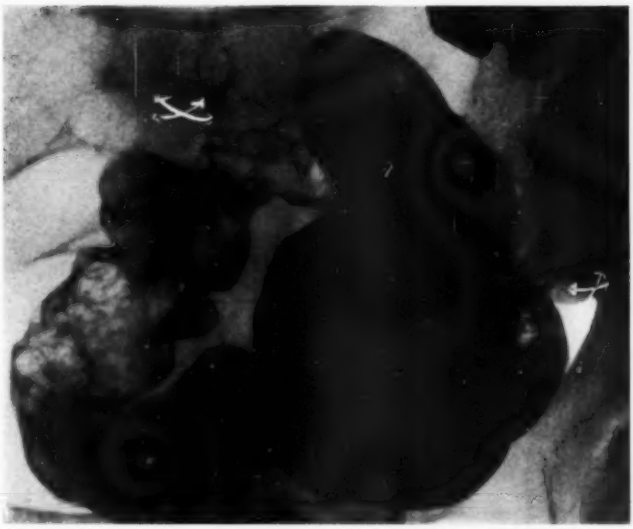

Fig. 1.

In such cases, the volvulus does not exceed 180 degrees, and as a rule the axial torsion is divided, so that mostly only a single, long axial torsion of about 180° can be demonstrated. Under such circumstances neither the volvulus nor the axial torsion offers any obstruction to the passage of the contrast fluid, and often they are found only during one of the phases of the examination, generally after part of the enema has been quitted.

Under certain conditions the axial torsion may become forcibly compressed to a shorter extent of the twisted loop, perhaps outside the involved portion of the latter; and, as first pointed out by GROTH, the lumen of the gut will then be more or less, if not completely, cut off, with resulting obstruction of passage and disturbances of nutrition in the gut wall and the mesentery. Such a compression of the axial torsion will be caused, for instance, by dilatation of the twisted loop. Though a volvulus of 180° does not cause actual obstruction, it may nevertheless become the cause of considerable obstipation in the loop involved. If the intestine as the result of this becomes dilated beyond a certain limit, it will first try to straighten out and thereby do away with the volvulus, which no doubt in many cases succeeds. But if such a spontaneous detorsion does not take place, for instance owing to too great rigidity of the abdominal wall, or too little space in the abdomen of some other

Fig. 2 a.

Fig. 2 b.

Fig. 3.

Fig. 4.

cause, the intestine will try to overcome the axial torsion (GROTH). This is not possible, however, as long as the volvulus exists; but as the intestine becomes more and more distended the axial torsion may become displaced until it to one side or the other meets a fixed portion of intestine, perhaps outside the length involved in the twist; which will then most often be on the afferent side. If the greater part or — theoretically — the whole of the axial torsion (that is, with a volvulus of 180°, from 180 to 360°) by this displacement becomes concentrated at one point, the result will be the cutting off of the lumen of the gut, as said above: perhaps resulting in complete obstruction (LAURELL's »torsion stenosis»). Many cases of acute volvulus no doubt develop in this manner.

Periodic, Spontaneously Remittent Volvulus

Besides a number of cases of symptom-free (»physiologic») volvulus and volvulus with the clinically well-known forms of ileus, we have in the last couple of years in the Roentgen Clinic of the State Hospital, among a large patient material (about 10,000 each year), seen at any rate 3 cases of frequently recurrent acute abdominal disorders, which it without roentgen examination was difficult, if not impossible, to diagnose with certainty; but of which there after roentgen inspection of the colon is little doubt that they are cases of periodically occurring, symptom-giving (»pathologic»), spontaneously reduced volvulus.

Case 1. — Woman, 32 years old, unmarried; admitted to the State Hospital (surgical service C) Nov., 1942. Since childhood very irregular stools, alternately hard and loose, but without slime or blood. In the last ten years attacks of pain in the right flank three or four times a month, radiating out over the abdomen, but not down towards the symphysis. The pain usually lasts without remission for up to twenty-four or forty-eight hours. It has no relation to meals or micturation. Food gives no relief; there is no nausea or vomiting. No icterus or febrilia. The patient says that the pain sometimes disappears when she lies down. It has become worse in the last year or so. About ten years ago, she was admitted to a provincial hospital, but the nature of her case could not be made out.

At the general examination (during a painless interval), nothing abnormal was found. *At roentgen examination of the colon*, with opaque enema, the rectum filled naturally, and then a very long sigmoid loop, the distal side of which lay to the left of the spinal column and did not turn over into the oral leg until away up in the epigastrium, which lay to the right of the spinal column and extended downwards towards the pelvis. At the level of the promontory, the lumen of the gut again crossed the midline, but here the enema encountered an obstruction, which it could not overcome. (Fig 5). Under continued attempts at injection of enema, the intestine became distended to the circumference of an upper arm, and in specially taken views the enema was seen to stop, with a regularly pointed contour, which curved slightly towards the concave side of the intestinal loop, reminding of the beak of a bird. This picture became still more distinct after part of the enema had been quitted (Fig. 6). It is typical of a volvulus where a part of the axial

Fig. 5.

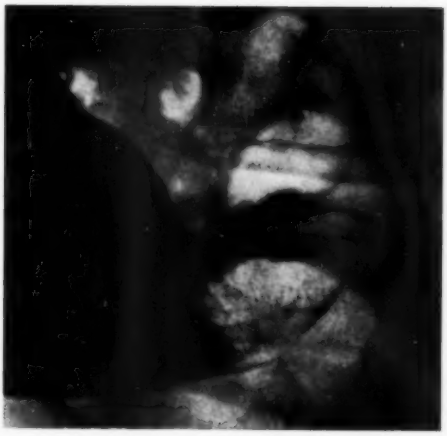

Fig. 6.

torsion is strongly compressed exactly at the point where the two legs of the twisted loop cross each other. There were no signs of ileus, and no further attempts were made to reduce the volvulus. The highly localized compression of the axial torsion must undoubtedly have been due, at least partly, to the injection of the enema. On renewed roentgen examination of the colon, five days later, it was found that the volvulus had become untwisted (spontaneously). The long sigmoid loop, which before the injection of the enema had been rather full of gas, now lay entirely in the right side of the abdomen.

From the result of these roentgen examinations, together with the clinical symptoms, it was believed that the patient's case could be explained as a periodically occurring volvulus of a long sigmoid, where dilatation of the twisted loop owing to meteorism or (and) coprostasis caused periodical, strong compression of the axial torsion and thereby further obstruction of passage, resulting in still greater dilatation and pain until the gut spontaneously became untwisted.

In view of the frequency of the attacks and the increasing intensity of the pains during these, *laparotomy* was done, under lumbar anesthesia (percain), with oblique incision in the left iliac fossa. The sigmoid lay right underneath; it was of the same large dimensions as seen at the roentgen examinations. In the mesentery, there were many old contractures, — signs of past cases of volvulus. At the moment, there was no twist in the intestine. It was drawn forwards for resection. Two days later, it was burned through; afterwards it was treated with Dupuytren's intestinal clamp, and two months later the colostomy was closed.

In reply to inquiry eighteen months later, the patient stated that since the operation she had not had pains in the abdomen. The stools are still a little sluggish, but her use of laxatives considerably less than before. She says herself that she is in excellent health. Directly questioned, she further states that the attacks of pain always had been accompanied by distension of the abdomen, which became hard to the touch; and that the

pain disappeared when she could get her bowels relieved and get rid of the gas in the intestine.

Epicrisis. — An unmarried woman, 32 years old, has for 10 years been troubled with attacks of acute abdominal pains, which after shorter or longer time cease spontaneously, especially when she lies down. Objectively, nothing can be demonstrated until roentgen examination of the colon shows an abnormally long sigmoid, which at the first examination is the seat of a volvulus without ileus, but with a greatly compressed axial torsion, which occludes the lumen of the gut. After this finding, the patient's case is believed to be due to periodic, spontaneously untwisting volvulus of the sigmoid; and at following operation this is confirmed by evidence of shrinking processes in the mesentery, as well as by the fact that there has been no recurrence of the abdominal pains since the long sigmoid was resected.

Case 2. — Woman, 37 years old, unmarried. Has for 2—3 years been suffering from frequent attacks of severe, colicky pains in the abdomen, across the epigastrium. They come on without any known cause; become worse when she moves, so that she is obliged to interrupt what work she is engaged in. When she lies down, the pain becomes less, sometimes after ten to twenty minutes, and always disappears entirely if she remains quietly on her back for a couple of hours (she has never tried lying on her side or on her stomach); but it returns if gets up again too soon, and may last a very long time if she does not get a chance to lie down. Between the attacks she is perfectly well. They come on at intervals of from a few days to several weeks, on the average once a week. They have no relation to the meals, there is no nausea, dysuria, icterus or rise of temperature. Her stools are mostly sluggish, and she then has to use laxatives; at other times there is diarrhea. During a period, two years ago, when the latter was the case, she was admitted to the State Hospital (service A), where nothing abnormal could be demonstrated after the diarrhea had ceased. After having had attacks of pain for three days, she was now, in February, 1943, re-admitted to the State Hospital, this time to surgical service C.

At the general, objective examination, nothing abnormal was found. *Roentgen inspection of the colon*, under injection of contrast enema, showed a long, looped sigmoid, on which there was an axial torsion, which became displaced upwards to the highest point of the loop, away up in the epigastrium, where it partly occluded the lumen of the gut and to some extent hindered the passage of the enema. After part of the latter had been quitted, the cause was seen to be a volvulus of the sigmoid colon, of at least 180°. At the injection, this had become partly straightened out when the axial torsion was displaced. After renewed injection of enema, and after the latter had been quitted, while the patient at the same time changed her position, the gut became entirely straightened out. Nothing in the roentgenologic picture suggested ileus.

From this, the patient's attacks of pain were judged to be due to frequently recurring, periodic volvulus of a long sigmoid, which spontaneously becomes untwisted when she lies down. Directly questioned, she explains that the pain always is accompanied by distension of the abdomen, so that her clothes feel tight, and that when it begins to abate it is always in connexion with a copious expulsion of flatus, which does not occur until she lies down. The patient was discharged without operation, and at the examination 1 year later it is found that the attacks continue unchanged.

Epicrisis. — An unmarried woman, 37 years old, has for 2—3 years been troubled with frequent attacks of intense colicky pain in the abdomen, which as a rule are eased and soon cease when she lies down, at the same time as there comes an abundant expulsion of gas from the intestine and the distended abdomen resumes its natural proportions. Her stools have as a rule been sluggish. A roentgen examination of her colon after a few

Fig. 7.

days marked by these attacks shows a volvulus of the sigmoid, which is very long. There are no signs of ileus, but a compressed axial torsion, which owing to the dilatation of the gut, causes rather considerable obstruction to the passage. The volvulus untwists when an enema is injected and the patient at the same time shifts her recumbent position. From these observations, the patient's attacks are judged to be due to a periodical volvulus of the sigmoid colon, which straightens out spontaneously when she changes her position. She is not operated upon, and the attacks continue as before.

Case 3. — Boy, 11 years old, admitted to the State Hospital (surgical service C) in January, 1943, with the diagnosis acute attack of chronic appendicitis. In the last six months he has had frequent attacks of pain in the right side of the abdomen; during the last month about 10, often accompanied by nausea, but no vomiting. Stools, flatulence and micturation said to be in good order. No increase of temperature in connexion with the attacks. The pains disappear spontaneously; sometimes, however, only after a few hours' rest in bed. Afterwards he is completely well. On the day of admission he had again had an attack, but severer than usual. His bowels had last moved the day before. Whether there had been flatus cannot be said. Temperature, 36.8° C. The abdomen soft; moderate tenderness in both iliac fossae, most in the right. Spontaneous discharge of flatus.

Roentgen examination of the kidneys, with intravenous urography, showed nothing abnormal. *Roentgen examination of the colon*, with opaque enema, showed a very long, mobile transverse colon, forming a large double loop, the midpoint of which lay away down in the left side of the small pelvis. The clearest picture of the condition was obtained after part of the opaque enema had been quitted. Then a volvulus of 180°, of the long loop of transversum, was distinctly seen, and just orally from the twist an axial torsion of about 360° (Fig. 7). There was no marked obstruction to inflow of the enema or to the evacuation of the intestine, and no signs of ileus. The attacks of pain were judged to be due to the observed condition of the colon, and it was believed to be a case of periodic volvulus. The patient was discharged without any causal therapy having been attempted. In reply to inquiry nine months later it was stated that he had not had any attacks since his discharge.

Epicrisis. — A boy, 11 years old, has for 6 months had frequent attacks of pain in the abdomen, which cease under rest in bed. Roentgen examination shows a volvulus,

of 180°, on a very long transverse colon, and immediately above this an axial torsion of about 360°. The case is judged to be one of periodically recurrent volvulus.

The pathologic picture in these three cases is almost identical, both as regards the for months and years frequently occurring attacks of abdominal pains, which come on suddenly and without apparent cause; and by the manner in which the pain as a rule can be made to cease when the patient lies down for a short time. Common for them all are moreover the practically negative result of the general clinical examination and the finding, on roentgenologic inspection, of a volvulus on an abnormally long colonic loop, without any signs of ileus, but with a very localized axial torsion; and that the volvulus either straightens out spontaneously or can be made to untwist by enema injection and by having the patient change position; or that at least the axial torsion thereby is loosened, so that passage through the intestine again becomes possible.

It seems natural to see a relation between the roentgenologic findings and the clinical symptoms; and the latter are of such a character that they may very well correspond to what would be expected in a case of volvulus of the type and degree here observed. It can therefore not be unreasonable to suppose that each of these attacks is the expression for an occurring volvulus, which perhaps does not begin to give symptoms until the moment when the axial torsion, owing to some cause or other, — for instance, dilatation of the gut, — becomes strongly compressed, resulting in more or less difficult passage, with further dilatation and pain. After this, the relief which all the patients are observed to obtain by change of position (when they lie down) must be supposed to be due to the volvulus becoming spontanoeusly untwisted, or at least the axial torsion slackened and perhaps later untwisting. That this is possible, is a well-known phenomenon, which, for instance, can be distinctly observed in cases of bloodless reduction of a volvulus under roentgen control (cf., among others, NORGAARD, 1944). It is probably also rather characteristic in this respect that two of the patients state that the attacks are accompanied by distension of the abdomen, and that the relief which they feel by lying down or by changing position is obtained at the same time as there is a copious discharge of flatus or feces. The cicatricial shrinkings of the mesentery found at the operation in Case 1 indicate that there had been many previous attacks of volvulus, and the good result of the operation, with resection of the long sigmoid, shows that the cause of the attacks had been localized to the latter.

In all three cases, the symptoms were so strongly pronounced that they gave occasion to thorough examinations after the patients' admission to the hospital, with the results stated. But as the volvulus evidently is only periodically present, and easily occurs and disappears

again, it will no doubt partly be a matter of chance whether the correct diagnosis can be made or not; because everything depends on whether volvulus and axial torsion, — or, at least, one of the two, — can be demonstrated at the roentgen examination. In a number of cases it must be expected that the result will be negative. The chance of a positive result will probably be greatest if the examination can be made during an attack.

The Symptoms in Colon Elongatum and Periodic Volvulus

In view of what has been said in the foregoing, there is reason for considering whether similar symptoms, in isolated attacks and perhaps in feebler degree, do not occur among other patients, without their cause being, in most cases, rightly understood. For purely mechanical reasons it must be among patients with a long, mobile colon that such cases should in the first place be looked for; and we know, in fact, already that an abnormally long colon may give rise to persistent, more or less greatly discomforting symptoms. Thus, in 1925, FLEMMING MØLLER collected 18 cases of greatly elongated colon and enumerated the symptoms accompanying that condition; which, in order of their frequency proved to be: persistent obstipation, sometimes alternating with diarrhea; abdominal pain, continuous or in sudden spells; meteorism and bleeding from the anus. FLEMMING MØLLER thought that part of the symptoms were due to torsion of the long loope of intestine or sharp bends in these. With our present better understanding of the mechanism of volvulus, and especially of the occurrence and significance of the axial torsions, more recent examinations of a number of cases of this kind lend strong support to his view. In remarkably many such cases, volvulus formation and axial torsion, — or axial torsion alone, — is demonstrated simultaneously with the presence of clinical symptoms of the kind just mentioned.

Case 4. — Man, 56 years old, whose defecation has for many years been difficult, and who has almost constantly had to use laxatives. On one occasion it seems that fresh blood was quitted per anum. In the last 3 weeks, the stools have been still more difficult, and there has been moderate pain in the left side of the abdomen. A roentgen examination at a private clinic, which he sought as out-patient, gave suspicion of tumor of the colon. The picture, which was kindly lent us, does not show any tumor, however, but on the long sigmoid loop a volvulus of 180°, and about midways on the twisted loop a compressed axial torsion of between 180 and 270°, with distinct obliteration of the lumen. The cause of the localized axial torsion has perhaps in this case been the clump of feces seen orally from the site of the torsion (Fig. 8), where it seems as if it were forcing the torsion farther along. — At renewed roentgen examination some days after the patient's admission a few days later, the gut was found to lie naturally, without any axial torsions.

The volvulus must thus have become untwisted spontaneously, or perhaps by the repeated injection of enema. At the same time, the pain had disappeared.

Fig. 8.

Case 5. — Man, 19 years old. Has in the last 5 years been troubled with rather uncharacteristic pains in the abdomen, without relation to meals; sometimes at night. His bowels move daily, spontaneously. During an attack of the usual pain, which had been lasting some hours, he is admitted, with the diagnosis: acute abdominal disorder. The general examination shows tenderness along the course of the colon, but otherwise nothing abnormal. With rest in bed, the attacks cease after a couple of days. Roentgen examination of the colon, 72 hours after admission, shows an abnormally long sigmoid with a volvulus of 180° and two axial torsions, which do not greatly hinder the inflow of the opaque enema. There are no signs of ileus. At an examination after barium meal a few days later (in continuation of examination of the stomach), the colon is lying naturally, and passage through the intestine is unobstructed.

Case 6. — Man, 44 years old. Has for twenty years been suffering from dyspepsia of uncharacteristic type; especially no resemblance to ulcer symptoms. It seems that in 1939 there has been melena. The stools are sluggish, but without fresh blood or mucus. He now complains of pressure in the epigastrium and pyrrhosis. Objectively, there is nothing abnormal; but roentgen examination shows a long sigmoid with a volvulus of 180°. On injection of the enema this becomes partly straightened out, but a highly localized axial torsion of fully 180° for a long while obstructs the inflow considerably, until the volvulus by continued injections, while the patient at the same time shifts his position, is entirely untwisted. After the defecation has been regulated, the trouble disappears.

Case 7. — Woman, 57 years old, who in the past has been three times laparotomised (epigastric herniotomy, salpingo-oophorectomy *cum* cholecystectomy, and another operation on the bile-passages). For 10—12 years pain in the left iliac fossa, radiating out into the flank. Also pain after defecation (»like labor pains»). Had once had to have a morphine injection for intestinal colic. The stools mostly thin, with mucus. Roentgen examination of the colon shows a distinct volvulus of the sigmoid, of 180°, and a rather long axial torsion of the descending colon, i. e. outside the area of the twisted sigmoid loop. The contour of the descending colon is smooth, indicating colitis (Fig. 9).

Case 8. — Woman, 76 years old, who in her youth has had gastric fever, and in whom there early was found achylia and in 1927 a megalocytic blood-picture and paresthesiae, for which she was treated with liver- and gastric preparations. From earliest youth she has suffered greatly with obstipation, for which she was repeatedly hospitalised; rectal stricture, among other things, being suspected. She is greatly troubled with

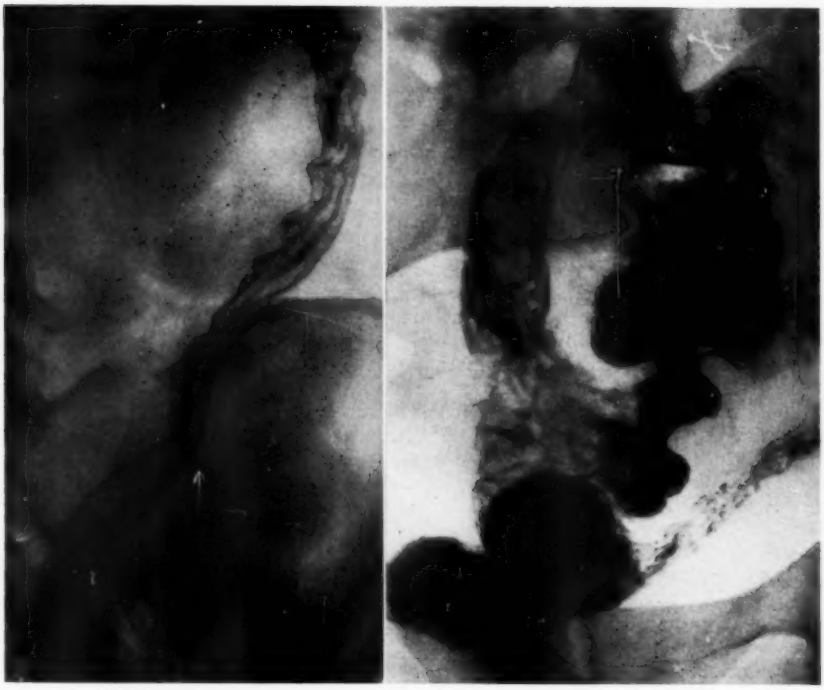

Fig. 9. Fig. 10.

meteorism, and intestinal borborygmus. Now, admitted to the State Hospital owing to fracture of the neck of the femur, she has, in spite of laxatives, had no bowel movements for five days, and at the same time her abdomen becomes distended. During the next days there is diarrhea, with as many as 10 stools in twenty-four hours and blood in the feces. Roentgen examination of the colon some time after shows a very long, looped sigmoid and a distinct, rather long axial torsion of the descending colon.

Case 9. — Woman, 38 years old. Has since her fourteenth year suffered from chronic obstipation accompanied by pressure, movements and rumbling in the abdomen. In the last years, periods of diarrhea, with pains about the umbilicus. No blood or mucus in the feces. Roentgen examination shows a very long sigmoid colon with smooth contours (colitis), and at the top of the loop a distinct axial torsion (? sharp bend).

Case 10. — Woman, 63 years old, formerly treated for a »gastric ulcer», of which there does not seem, however, to have been any sure diagnosis. Since youth she has been troubled with difficult defecation, with alternately hard and loose stools. For some years she has had pinching pains in the abdomen, especially in connexion with diarrhea; and several times she has noticed blood in the feces. Roentgen examination of the colon shows an abnormally long sigmoid, and after part of the opaque enema has been quitted an axial torsion of about 180° is seen on the splenic flexure.

Fig. 11.

Fig. 12.

Case 11. — Woman, 46 years old. Has for many years suffered from persistent obstipation. There are often several days between the stools, and besides she is troubled with borborygmia. Moreover, she suffers from hemorrhoids and frequent bleedings from the anus. For many years she has also had frequent attacks of abdominal pains, which were interpreted as due to gallstone; but roentgen examination of the bile-passages, with cholecystography, showed normal conditions. At the objective examination, a number of hemorrhoidal tumors are found about the anus, and also a ring of small internal hemorrhoids, for which she does not wish to be treated. Roentgen examination of the colon shows a very long sigmoid, which, after part of the opaque enema has been quitted, lies with a volvulus of 180°, and a distinct axial torsion, also of 180°, at the top. (Fig. 10).

Case 12. — Man, 62 years old, on whom total laryngectomy has been done, for cancer. During his following confinement to bed, phlebitis of the lower extremities developed; and besides, his defecation became difficult and there was considerable meteorism, but no pains or vomiting. As ileus was feared, a roentgen examination of the abdomen was made, with injection of opaque enema. There were no signs of ileus, but on the very long, looped sigmoid a volvulus of about 180°. This was partly straightened out by the injection of the enema, but only by simultaneous displacement of an axial torsion which, as a result of this, completely occluded the lumen of the gut, resulting in the characteristic roentgenologic picture (Fig. 11). Under continued injection and simultaneous shifting of the patient's position, both the volvulus and the axial torsion were finally untwisted. In the following days there was several times positive benzidine

reaction in the feces. We were later told that the patient also before his hospitalisation had been much troubled with meteorism.

Case 13. — Woman, 49 years old. Not less than fifteen previous hospitalisations, during which she had had a stomach operation and had been operated on for salpingitis and for adhesions. Her bowels have »always» moved very sluggishly; there has sometimes been as long as two weeks between defecations; but she has only now and then had resort to laxatives. Ten days before her present admission she had fallen from a kitchen table and had sustained a trauma of her abdomen, across the symphysis, by knocking against the edge of a chair. Since then she has had pains, diarrhea and vomitings. She is admitted for ileus. On examination, her abdomen is found diffusely distended and tender; now and then there is a slight bulging of the bowel. Roentgen examination with contrast enema shows an as a whole extremely long, very looped colon, on the sigmoid part of which there is a rather short volvulus with, at any rate, one highly concentrated axial torsion, which only with some difficulty is passed and partly loosened. Altogether, it is almost impossible to make the different parts of the long colon out from each other in the roentgenograms. As the attacks are rather mild and of short duration, and the patient's general condition contraindicates the contemplated operation (resection of the sigmoid), she is, on account of anemia, transferred to the medical ward, and from there, later, to the psychiatric ward, for mental disease.

Case 14. — Woman, 21 years old. As child and in early youth she was nervous and psychoneurotic. Since 1939, she has twice been admitted to hospitals in the provinces, for dyspepsia, chronic obstipation and emaciation. It seems that during these hospitalisations »megacolon» and sigmoiditis were demonstrated. She has now for some months been suffering from fatigue, loss of weight, persistent diarrhea alternating with hard, sluggish bowels, vomitings and pains in the left iliac fossa. She is admitted with the diagnosis: intestinal tuberculosis. The general clinical examination shows nothing particular. Roentgen examination, with contrast enema, shows an as a whole very long colon, of which the transverse part, especially, impresses one by its abnormal length; its right and left sides lie as a double loop, with a volvulus of 180°, in the middle of the abdomen. The enema only with difficulty passes a compressed axial torsion at the aboral end of the twisted loop (Fig. 12); but by repeated injections, during which the patient is made to shift her position in various ways, the passage is finally effected, and after part of the enema has been quitted the volvulus is untwisted.

Though the occurrence of symptom-free, »physiologic» volvulus, as said in the beginning, is rather frequent in patients with an abnormally long colon, there are good reasons for believing that the symptoms in the last cases here described (Cases 4—14) were for a great part due to the simultaneously demonstrated changes in the position of the patients' colon. In contrast to what is the case in physiologic volvulus, there was thus in several of these cases more or less obstruction to the inflow of the enema into the intestine, mostly due to very localized (compressed) axial torsions, and often considerable difficulty in getting the volvulus straightened out. The same is probably the case as regards the natural passage through the gut and the possibility of spontaneous untwisting. The symptoms also resemble, though in a milder degree, those in the first three cases described (Case 1—3), which, as said, can

with almost absolute certainty be ascribed to periodic volvulus. The transition between the cases of the two groups, is in fact, extremely fluid. At any rate, the colitis undoubtedly present in some of the cases cannot account for the symptoms in all the cited cases of abnormally long colon, and the latter may very well itself be secondary to the periodic obstipation and obstruction caused by the attacks of volvulus. Where symptoms such as those described occur in a case of colon elongatum, and nothing else abnormal can be demonstrated in the intestine, there are good reasons for assuming that they are due to changes in the position of the long, mobile intestinal loop, causing periodic volvulus and compressed axial torsions of the latter.

The question is not merely of theoretical interest; for the correct understanding of the pathogenesis of the cases plays a rôle for their effective treatment. Thus, obstipation and meteorism in the case of an abnormally long colon may, if no treatment is instituted, be the cause of a symptom-free, physiologic volvulus becoming symptom-giving in the manner described; and if this happens repeatedly the result will be the occurrence of the well-known mesosigmoidal shrinkings and cicatricial changes in the root of the mesentery; whereby the tendency to fresh attacks of volvulus is increased; and in the further course the result will then either be acute volvulus, with ileus, or symptoms like those already described in connexion with colon elongatum, intensified from time to time, or perhaps severer attacks like those in cases of periodic, spontaneously untwisting volvulus (Cases 1, 2 and 3).

In these severest cases, the general condition and working capacity of the patients are affected to such an extent that even operative treatment may be indicated; and under such conditions the right understanding of the causes of the trouble is, of course, of paramount importance. One of the cases in which operation was performed (Case 1) shows the good result of such treatment. One of the other cases (Case 3) seems to show that the attacks may cease spontaneously; but the observation time in this case is yet too short, and perhaps also the fact that the patient was a child may have something to do with the matter. Also in Case 2 it will no doubt eventually be necessary to operate, if the attacks continue with the same frequency and severity, as seems to be the case. And, as the passage of a for many years unrecognized case into a chronic state of invalidity shows, the adoption of such a therapy should not be postponed too long, either in favor of conservative, symptomatic treatment or in hope of spontaneous restitution.

Case 15. — Woman, 39 years old, unmarried, admitted in 1940 to the State Hospital (surgical service D). Has never been pregnant and denies venereal diseases. Her bowels have always acted sluggishly and have had to be kept in order with laxatives, but otherwise her general health has been good until 1936, when her present affection

began with intenser attacks and constant grumbling in the right side of the abdomen, accompanied by moderate increase of temperature. The attacks were interpreted as due to salpingitis and parametritis, and in the past four years she has on their account been confined to bed ten times for rather long periods. Thus, two years ago she was for five weeks in a Copenhagen hospital, where she was treated for right-side salpingitis. Very short time after her discharge she was re-admitted to the same hospital, with acute aggravation of the symptoms, and was then operated on for appendicitis, — but without any effect on the symptoms. After two-three months of constantly increasing symptoms and slight fever, for which she had been confined to bed at home, she was now examined in a clinic for women's diseases and from there admitted to the State Hospital (surgical service D), for acute febrile salpingo-oophoritis.

Her menses had in the last five years been perfectly regular, and there had been no aggravation of the abdominal symptoms in connexion with them; only a very slight amount of whitish vaginal pus. No urinary symptoms. At the gynecologic examination, a moderate tightening was found in the right side of the small pelvis, which drew the uterus a little toward that side. Examination of a sample of secretion from the cervix and urethra was negative for gonococci. Also Wassermann and gonococcus reactions were negative. After three weeks' confinement to bed and thermotherapy, the tightening could no longer be felt; but the patient stated that the symptoms were still the same. On account of the sluggish bowels, she was now referred for *roentgen examination of the colon*. The injected contrast enema soon filled a large sigmoid loop containing a considerable amount of gas. It gradually became rather strongly dilated; the patient in the meantime stating that her abdomen was feeling tense, and it proved quite impossible to force the enema farther along, into the descending colon (Fig. 13). She was now allowed to quit the greater part of the enema, and thereby a little of it was pressed into the distal end of the descendens, where a considerable coprostasis was seen. At the same time, a distinct volvulus of the sigmoid was disclosed, with several prominent, tight axial torsions, which in part became still more distinct at renewed attempts to overcome the obstruction by injections of enema (Figs. 14 and 15). The volvulus was undoubtedly of 180°, but the combined degrees of the axial torsions exceeded the 360° corresponding to this; which was probably due to combination with twisted, sharp bends in the sigmoid, the upper, greatly dilated part of which was sunk downwards anteriorly. (For details respecting this, see NØRGAARD, 1941).

On account of the roentgenologic findings and the continuous pain, a laparotomy was done, and corresponding to the result of the roentgen examination, a volvulus of 180° was found on the sigmoid colon, which was easily rotated back. The mesentery was the seat of very marked mesosigmoidal changes, with strong contractions which had to be severed before the gut could be fixed to the abdominal wall. In the pelvis, the uterus and its annexa felt natural.

At an after-examination two months later, the patient's condition was much improved. There were no longer any attacks of pain, and she did not of herself complain of anything; but when questioned she said that there was a feeling of pressure in the left iliac fossa. Recto-vaginal exploration showed nothing abnormal. In reply to inquiry two years later, she stated that she had some attacks of abdominal pains, but not of the same character as before, and that there had been no need of hospitalisation.

In this case, there is hardly any doubt that the patient's abdominal pains, at least during the time immediately before the operation, were due to a periodic compression of the axial torsion in the chronic volvulus; which probably itself in the beginning has been periodic, spontan-

Fig. 13.

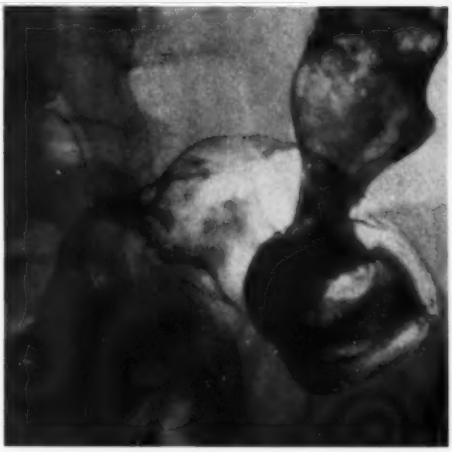

Fig. 14.

Fig. 15.

Fig. 16.

Fig. 17.

eously reducible, but has later become unable to untwist spontaneously, owing to the changes in the mesentery. The pains in the time after the operation, which were not as intense as those before, may perhaps have been due to the same mesenterial changes, since no resection was made, as in Case 1.

Anyhow, a chronic volvulus does not necessarily give rise to very marked symptoms; as seen, for instance from the case described by HOLMGREN, to which reference has been made in the foregoing. Also among our patients we have had such a case, in which the symptoms, despite the almost monstrous intestinal changes resulting from it, were not particularly alarming.

Case 16. — Man, 64 years old, admitted to the State Hospital (service H) in 1942, for varicose ulcer of the leg. In 1897, he had had meningitis, and in the following time there slowly developed spastic paresis of the right upper and lower extremities, probably as result of an atrophic process in the left hemisphere following the meningitis. At the general clinical examination, a large tumescence was felt in the right side of the abdomen,

from the right iliac fossa to up underneath the right thoracic margin. Its character could not be made out; it persisted unchanged after catheterisation of the bladder.

Roentgen examination of the abdomen (without contrast enema) showed the latter filled with large gas-distended loops of the colon, full of feces. An enormously broad loop in the right side was particularly noticeable; in the roentgenogram it measured about 20 centimeters in breadth and was almost entirely filled with a massive lump of feces larger than the head of a child (Fig. 16). It could not be seen with certainty whether there was gas also in the loops of the small intestine. In pictures taken with the patient in standing position, no fluid levels were seen. When injection of opaque enema into the colon was attempted, the rectum filled readily; but at the junction of the sigmoid there was a point where the lumen was somewhat smaller and the passage rather difficult. After a little while the enema broke through, though; whereupon it filled the greatly distended loop of the colon just mentioned, which proved to be an enormous sigmoid, occupying the greater part of the right side of the abdomen. Under continued injection also the descending colon filled. This, too, was long, and formed a double loop in the left side, in towards the middle of the large sigmoid (Fig. 17). By this time, between five and six liters of enema had been injected, and the abdomen, had become so distended that no more fluid could be forced in. Therefore, the transverse and ascending colon could not be filled; still, both these sections were seen fairly distinctly in the roentgenographs taken without contrast enema.

Fig. 18.

Both at the screening and in the films it was seen that the difficult passage at the junction of the rectum and the sigmoid was due to a volvulus of at least 180°, with an axial torsion, also of 180° (Fig. 18). Also at the junction of the sigmoid and the descending colon the passage was for a distance a little difficult, and one had the impression that there here, too, was a slighter, and especially less compressed axial torsion; which could not, however, be clearly visualized in the roentgenograms, because the area could not be projected free from the other loops of the intestine.

A rectal sound was now introduced, and was carried along up past the site of the volvulus, in order to get the latter straightened out. But all attempts at this were in vain, undoubtedly because the large coprolith held the gut immovable in the twisted position. Whereas the patient had hitherto said that his bowels had been kept in order by means of laxatives, it now appeared that he often had been completely obstipated for several days in succession, whereupon there had frequently been diarrheas. During his stay in the hospital, his bowels had most of the time moved spontaneously, with »formed» feces; only now and then had it been necessary to use »pills». After he had been

roentgenographed, it was tried to get the coprolith dissolved by means of oil clysmas; it became somewhat smaller, but could not be removed by that means.

A roentgen examination 10 days after the first showed that the coprolith in the sigmoid had become somewhat smaller, and that there now in the rectum was another, the size of a goose's egg (part of the first). They lay on each side of an axial torsion of 180° at the junction of the rectum and the sigmoid. Neither on this occasion was it possible to get the gut untwisted by injection of enema and shifting the patient's position.

It is difficult to say with certainty what the mechanism of development has been in this case, where the volvulus had presumably existed a long time. But also here it has probably been a case of an originally »physiologic» volvulus, which had not hitherto given rise to any symptoms, but which then, owing to some cause or other, has not become untwisted and has then caused greater obstipation, with resulting formation of coproliths. I may here point to the two cases no. 8 and no. 12, in which confinement to bed for some cause or other, immaterial in this connexion, of patients with an abnormally long colon disposing to physiologic volvulus, became the cause of greater obstipation and thus to attacks of symptom-giving volvulus. The case here described again emphasizes the importance of getting these cases treated in an early stage by trying to counteract obstipation and meteorism; as, otherwise, the result may be the development of a *circulus vitiosus* with continually increasing symptoms.

SUMMARY

After briefly mentioning the well-known considerable difference in the degree of the symptoms in cases of volvulus of an abnormally long colon, the author relates 3 cases, in which the severe abdominal symptoms present must be supposed to have been due to the periodical formation of a spontaneously reducible volvulus, or perhaps to periodic shortening and slackening of an axial torsion from an otherwise symptom-free volvulus. The general clinical examination discloses nothing abnormal except some tenderness of the abdomen, but the symptoms are rather characteristic and the roentgen examination shows after the attack a volvulus with more or less compressed axial torsions on an unusually long colon. A fourth, for many years misinterpreted case is given, in which the patient has by now become to a great extend an invalid.

In connexion with this, the author relates a series of cases of colon elongatum; and on account of the similarity between the clinical symptoms in these and the symptoms in the cases described, and the frequent finding of volvulus and axial torsions at the roentgen examination, he points out that our present, increased knowledge of the mechanism of volvulus strongly supports the theory emitted by FLEMMING MØLLER already in 1925, that the symptoms in colon elongatum are due to torsion or a sharp bend on the intestine.

Finally, a case of chronic volvulus of the sigmoid colon, resulting in monstrous changes, is described.

ZUSAMMENFASSUNG

Nach kurzer Erwähnung der wohlbekannten, bedeutenden Unterschiede des Grades der Symptome bei Fällen von Volvulus eines abnorm langen Kolons, berichtet Verf. über 3 Fälle, bei denen die vorliegenden schweren Bauchsymptome als durch periodische Entstehung eines spontan sich lösenden Volvulus bedingt anzusehen sind, oder vielleicht durch periodische Spannung und Erschlaffung einer axialen Drehung eines sonst symptomlosen Volvulus. Die allgemeine klinische Untersuchung zeigte nichts Abnormes, ausser einer gewissen Druckempfindlichkeit des Bauches, doch sind die Symptome recht charakteristisch, und die Röntgenuntersuchung zeigt nach einem Anfall einen Volvulus mit mehr oder weniger komprimierten axialen Drehungen eines ungewöhnlich langen Kolons. Es wird ein vierter, viele Jahre lang falsch aufgefasster Fall wiedergegeben, wo der Kranke schliesslich in hohem Grade Invalide geworden war.

In diesem Zusammenhange berichtet Verf. über eine Reihe von Fällen von Colon elongatum, und auf Grund der Ähnlichkeit der klinischen Symptome dieser Fälle mit den in den beschriebenen Fällen vorliegenden Symptomen sowie des häufig erhobenen Befundes von Volvulus und axialer Drehungen bei der Röntgenuntersuchung, macht er darauf aufmerksam, dass unsere jetzige, vermehrte Kenntnis des Mechanismus des Volvulus eine starke Stütze für die von FLEMMING MØLLER bereits 1925 aufgeworfene Theorie darstellt, dass die Symptome bei Colon elongatum durch Drehung oder scharfe Knickung des Darmes bedingt sind.

Schliesslich wird ein Fall von chronischem Volvulus des Colon sigmoideum, der monstruöse Veränderungen herbeigeführt hatte, beschrieben.

RÉSUMÉ

Après avoir rappelé brièvement le fait connu de la très grande différence dans l'intensité des symptômes dans les cas d'iléus frappant un colon de longueur anormale, l'auteur rapporte trois cas dans lesquels il faut admettre que les très graves symptômes abdominaux relevés ont dû provenir de la formation périodique d'un volvulus spontanément réductible, ou peut-être du raccourcissement et du relâchement d'une torsion axiale dans un volvulus d'ordinaire sans symptômes. L'exploration clinique générale ne révèle rien d'anormal sauf une légère sensibilité abdominale, mais les symptômes sont plutôt caractéristiques et l'examen radiologique révèle après la crise un volvulus avec des torsions axiales plus ou moins comprimées sur un colon de longeur anormale. L'auteur relate un quatrième cas ayant donné lieu quatre ans durant à des interprétations erronées dont le porteur est, à un haut degré, actuellement affecté d'invalidité.

L'auteur achève son étude en exposant une série de cas d'élongation du colon; se basant d'une part sur l'analogie entre les symptômes cliniques qu'ils présentent et ceux des cas décrits, et, d'autre part, sur la fréquence du volvulus et des torsions axiales à l'examen radiologique, il souligne que notre connaissance présente plus complète du mécanisme du volvulus fournit un sérieux appui à la théorie émise dès 1925 par FLEMMING MØLLER, suivant laquelle symptômes de l'élongation du colon sont dus à une torsion ou à une courbure à angle aigu de l'intestin.

Il termine en décrivant un cas d'iléus chronique du colon sigmoide résultant de la présence d'une monstruosité.

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FROM THE ROENTGEN CLINICS OF THE VIBORG TOWN AND COUNTY HOSPITAL AND THE KJELLERUP HOSPITAL, DENMARK (CHIEF: KRISTIAN OVERGAARD)[1]

ON BECHTEREW'S DISEASE FROM THE ROENTGENOLOGIC POINT OF VIEW[2]

by

Kristian Overgaard

Ankylopoietic spondylarthritis, or Bechterew's disease, was first described as a separate pathologic entity by that author, in 1892. As its principal characteristics, BECHTEREW named the kyphosis and the absolute fixation of the spinal column. In several following papers he elaborated the description, and accompanied it with a report of the necropsy findings in a single case. About at the same time there appeared descriptions, by STRUEMPEL (1897) and PIERRE MARIE (1898), of a pathologic picture which shows considerable resemblance to the cases described by BECHTEREW, but also in several respects differs from them; thus, there was, instead of the kyphosis, a noticeable flattening of the back, and, besides the affection of the latter, an affection of hip- and shoulder joints, which finds expression in PIERRE MARIE's designation for the disease: *spondylose rhizomélique*.

About the beginning of the century there appeared several reports of isolated cases; but from the different communications it can be seen how difficult the diagnosis was at that time, because it was hardly possible always to distinguish with certainty between ankylopoietic spondylarthritis and simple degenerative spondylosis deformans. A couple of studies by E. FRAENKEL (1904, 1907) are particularly valuable, because he, as the first, lays stress on the ankylosis between the articular processes as the characteristic for the affection, while he attaches less importance to the ossification of the anterior longitudinal ligament. Besides, he lays stress on the ankylosis in the costovertebral joints and in one

[1] The greater part of the material mentioned in this study is referred from the People's Sanitarium of the Danish Red Cross at Hald. For permission to make use of the records and films of these cases, as well as for hearty, good collaboration, I thank the head of that institution, senior physician, Dr. HOLGER JACOBSEN.

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instance mentions the synostosis of the iliosacral joint. In 1930, EHRLICH gave a detailed description of the disease, based on a very large material (753 cases) from the German People's Insurance. In the last ten years the disease has been the object of greater attention. Not only has it been found to be more frequent than hitherto supposed, but the physicians have learned to recognize it in earlier stages than formerly, and also the prospects of a passable result of its treatment are better to-day.

Ankylopoietic spondylarthritis must be considered as an infectious disease of rheumatic character, which affects the whole organism, but in which the changes are localized particularly to the bones and joints of the vertebral column. In the early stages it can often present difficulties for the diagnosis, but in fairly pronounced cases it shows a number of very characteristic features, both clinical, pathoanatomic and roentgenologic, which clearly distinguish it from the other rheumatic affections. The etiology is unknown. As with rheumatic polyarthritis, it is in some cases likely that a preceding angina has opened the way for the infection; in other cases no such initial disease can be demonstrated, and several authors have therefore ascribed an etiologic significance to different »hidden foci», which, however, is denied by others. As the disease is most frequent in men, gonorrhea has by some been considered as an essential causative factor (FORRESTIER), but for this there does not, according to more recent investigations, seem to be any foundation. The majority of the patients have for a considerable preceding period been suffering from indefinite »rheumatic» troubles. A hereditary factor may probably play a rôle for the development of the disease. In two of the cases observed by me, the father of the patient was similarly affected, in a third a twin-brother and the mother, in a fourth a brother. To what extent occupation and external influences play a rôle is uncertain. It is true that EHRLICH's statistics show a preponderance of patients from the hard-working classes, but the difference is not great, and the possibility of effects from the war cannot be excluded.

The overwhelming majority of those attacked by the disease are young men; in the large statistics the female patients constitute only 2 to 3 per cent of the cases. In most of the men the disease has begun insidiously between the ages of 20 and 30. The first symptoms are most often rather indefinite pains in the loins, higher up in the back or in the back of the neck. The pains are rather uncharacteristic, most nearly something like myalgia. In the beginning they are only felt when the patient moves, but later they may come on also when he is at rest or in the night. The lumbar pains may radiate out towards the ischial or femoral regions, but only rarely have the character of an ischialgia. Simultaneously with the pains there comes an incipient stiffness of the back, as a rule most strongly developed in the lumbar region. In many cases this stiffness does not

discomfort the patient to any great extent, however, and is paid no attention to until at a rather late stage.

In a number of cases the later course is marked by the appearance of pains in the hip- and shoulder-joints, and also other articulations, for instance the knee- and mandibular joints, may become involved. Also these may become stiff, with the result that walking becomes extremely difficult and painful.

The objective examination as a rule shows, already in an early stage of the disease, a marked flattening of the vertebral column, most pronounced in the lumbar region; later, but less constant, also in the thoracic. In the latter there can, however, in many cases develop a considerable, rather high situated, arcuate kyphosis. Such a development, though, is probably not so much a characteristic feature of the disease as it is due to fixation of the vertebral column in an awkward position.

Already in the incipient cases there is marked stiffness of the vertebral column, often most pronounced in its lower part; while the regions higher up often for a longer time preserve a slight mobility. In more advanced cases the stiffness is, on the other hand, very pronounced. When the body is bent forwards, the whole pelvis follows, and the whole movement takes place in the hip joint. The floor can only be reached by the patient bending both in hip and knees. Also when he bends sidewards, the pelvis follows the movement, and at any slight sidewards inclination the opposite foot is lifted from the floor. At rotatory movements, the whole body follows. This marked stiffness as a rule develops first in the lower portion of the vertebral column, and in a number of cases there may still after a long time be fairly good mobility in the cervical region, specially of the nodding movement in the atlanto-occipital and the atlanto-epistropheal joint.

At the same time as the vertebral column thus becomes stiff, there occurs a fixation of the ribs in the costovertebral and costotransverse joints, as a result of which the movements of the thorax become minimal and the respiration entirely of the abdominal type.

In the early stages there is often distinct tenderness to tapping on the spinous processes or the vertebral arches, or indirect tenderness on pressure on the head. Often there is also a marked tenderness localized to the muscles of the back. In the later stages with distinct fixation of the vertebral column there is in most cases considerable atrophy of these muscles, and also the intracostal muscles are mostly atrophic.

In severe cases, where, besides the back, also the shoulder or hip joints, or perhaps other articulations, are involved, there is tenderness over the affected joints and spasms of the surrounding muscles, and tenderness of these and of the corresponding tendons and their attachments.

The patients in these cases are mostly thin and of the asthenic type. As a rule, they are pale, and examination of their blood may show slight anemia; but often the conditions are found to be normal. As in polyarthritis, there is often moderate lymphocytosis. The sedimentation reaction is nearly always distinctly increased, greatly in fresh, moderately in older cases. The temperature is stated to be often slightly increased in the early stages, in the later it is normal. In the early stages there is also often a considerable tendency to transpiration.

As in other rheumatic diseases, there are often affections of the heart, either endo- or myocardiac. Also rheumatic arthritis or chorioiditis is frequent in the anamnesis.

BECHTEREW originally believed the disease to be an affection of the nerves, but according to what we now know about it the nervous symptoms play only a minor rôle. They consist chiefly in pains localized to the ischiadic and femoral regions and in costal neuralgias. These neuralgic pains often become projected to interior organs and give rise to mistaken diagnoses by simulating renal, abdominal or cardiac affections. Now and then neuritis may occur, determined by extension of inflammatory processes to the nerve branches, whose dorsal ramifications in the thoracic and cervical regions pass very close to the intervertebral articulations.

Since the affection is not in itself lethal and chiefly attacks individuals in the younger age classes, the cases that come to pathoanatomic examination will most often be far advanced. There will then, as a rule, be found osseous ankylosis of the intervertebral joints in the whole vertebral column, or, at any rate, in the greater part of it, and in most cases also of the costovertebral and costotransverse joints. Also ankylosis in the iliosacral joint is a rather constant finding. But besides these changes there is very often extensive intervertebral ossification of the ligaments of the vertebral column, changes in the intervertebral disks and osseous changes in the vertebrae.

Owing to these severe changes, which represent the terminal phase of the disease, there is little opportunity for forming an estimate respecting the development of the affection. It is therefore fortunate that descriptions exist of a small number of cases which were examined in a comparatively early stage (SIVEN, 1903; GUENTZ, 1933; KLINGE, 1934).

From the findings of these authors it appears that the earliest demonstrable phenomenon is arthritis of an inflammatory character in the intervertebral joints; there are accumulations of lymphocytes in the synovial membranes, and from the border of the joints a pannus grows in over the partly degenerated intervertebral cartilage, destroying it from the surface; and also the osseous surface of the joint is superficially arroded. Gradually, the whole joint becomes filled with such

granulation tissue, and this is transformed into a more fibrillar connective tissue. In this fibrous ankylosis, a development of bone takes place by invasion of osseous tissue from the surfaces of the adjoining bones and from the borders of the joint, and thus the ankylosis becomes osseous. This development takes place gradually, and both in the fibrous and the osseous ankylosis there may be lying remnants of the normal joint-elements: islands of undamaged cartilage or perhaps cartilage-covered remnants of the free joint cavity (KREBS; according to WURM). In the osseous ankylosis there may, besides, be cicatrices from connective tissue.

In the cases examined, the degree of development of the articular changes was more or less the same in most of the intervertebral joints. They seemed to be somewhat more advanced than in the costovertebral and costotransverse joints; but the changes in these were of the same character.

With regard to the iliosacral joints in the early stages of the disease no examination has been made; but the roentgenologic findings make it reasonable to suppose that changes of a similar character set in at an early period also there.

In the more advanced cases with osseous ankylosis there is most often found a development of bone also in the ligamentous apparatus of the vertebral column. This new bone formation is of various intensity and extent in the different ligaments; most frequent and as a rule most developed, in the ligamenta flava, especially in their lateral part, which lies near the intervertebral joint. It is also frequent in the inter- and supraspinous ligaments; whereas the ligamenta intertransversaria relatively seldom undergo osseous transformation.

Also in the anterior longitudinal ligament there is frequently seen a similar transformation, which is stated most often to begin in its lateral part, close to the roots of the arches (WURM). The degree of the development can vary a great deal, from fine, superficial osseous streaks in the otherwise fibrous ligament to a massive shell of bone covering both the bodies of the vertebrae and the intervertebral disks. From GUENTZ's studies it appears that this osseous transformation begins in the ligament itself but rather soon at the level of the intervertebral spaces involves the fibrous elements of the disk (the annulus fibrosus), whose superficial layers become osseously transformed. After a development of connective tissue has replaced the fibrocartilaginous, this formation of bone can gradually extend to deeper and deeper layers.

The cause of this bone formation is uncertain. Some authors speak of a special tendency to ossification of the connective tissue in these patients, owing to a »fibrositis» or something of that kind; others think that the osseous development is secondary and takes place in the liga-

ments which have undergone degeneration as result of the fixation of the vertebral column. GUENTZ is the only one who has examined this matter histologically. He says that no signs of inflammatory processes can be demonstrated in the ligaments, but that there in these is seen a deposition of calcareous matter, the place of which is later taken by new formed osseous tissue. This negative finding does not altogether exclude the possibility that the depositions of lime may be due to a preceding inflammation; because rheumatic foci in rather short time may become the seat of such (KLINGE). That the osseous changes as a rule occur chiefly in the parts of the ligaments nearest to the affected joints (WURM) would seem to indicate that the changes are of inflammatory character; but until the matter shall have been studied further we must consider this question as unsolved.

At the same time as these changes take place, the fibrocartilaginous tissue in the central part of the disks degenerates, probably owing to failure of the fluid-supply by which the avascular tissue is nourished, and which normally is maintained by the movements of the vertebral column. From the upper and nether surfaces of the vertebrae, streaks of connective tissue and bone then invade the degenerated tissue of the disks, supplanting it partly or entirely. That the vertebral interspaces do not become narrowed, as it is the case in simple fibrous degeneration, is probably because the distance between the vertebrae has by that time become fixed as result of the articular and ligamentous changes.

In the cases where there is marked osseous transformation of the ligaments, changes are often seen in the bony structure of the vertebral bodies. The cortex, especially anteriorly, but also along the sides, becomes thickened, and at the same time the central part of the bodies becomes rarefied. Together with the ankylosis of the intervertebral joints and the ossification of the ligaments of the arches, this transformation gives the entire vertebral column a structure reminding of a long tubular bone; a formation to which the ankylosed vertebral column statically is analogous.

Frequently the pathoanatomic examination also discloses other signs of rheumatic affections: pericardiac changes, rheumatic cardiac affections, and affections in other joints (shoulder, hip, knee) corresponding to rheumatic polyarthritis; and the disease is probably with good reason considered to be a rheumatic affection, though the question of its exact place in the rheumatic system is not finally settled.

As it might be expected, the pathoanatomic findings agree fairly well with the roentgenologic picture; but in several respects there is nevertheless an apparent disagreement; which may be due partly to the fact that pathoanatomic changes, even when they are fairly pronounced, only to a slight extent are capable of altering the roentgenologic ap-

Fig. 1. Ileo-sacral joint with initial changes (Stage I). The articular surfaces are on the left side slightly blurred, on the right the articular designs are somewhat more effaced. Osseous deposits with sharp outline, similar to an exostosis at the anterior superior iliac spine. Further a solitary intervertebral bone-formation between the fourth and fifth lumbar vertebrae. (Case 6. — Subjective symptoms for about 6 months).

pearance of the bones and joints, partly to the manner in which the roentgenologic picture reveals changes to which the pathoanatomy has not attached essential importance.

In the early stages, the disease is difficult to recognize roentgenologically, and the changes in the vertebral column itself, — to which the patient refers his complaints, — are often slight and rather uncharacteristic. For the question of the diagnosis it was therefore a great step forward when KREBS in 1930 pointed out that there in this disease often are roentgenologic changes in the iliosacral joint. That this is so has since been confirmed by SWAIM & KUEHN (1932), BUCKLEY (1935), SCOTT (1936), LASSEN (1939), FORRESTIER (1939) and EBBENHORST TENGBERGER (1941), who all affirm that these changes are a very early, very constant and characteristic finding.

The changes manifest themselves, early in the disease, in the form of scattered, slightly cloudy opacities in the osseous tissue about the iliosacral joint. At the same time there is a slight, spotty decalcification of the subchondral osseous tissue, also with very vague and blurred demarcation (Stage I). Confluence of several small rarefactions may result in apparent increase in the width of the articular interspace, — according to FORRESTIER most often of its lower part. At the same time as the decalcification spreads in some places, the compactness becomes greater and more extensive in others, and in several places small bridges of compact osseous tissue are sent across the articular interspace (Stage II). As the disease gradually advances, the new bone formation prevails, and the articular design is effaced by a new-formed, slightly com-

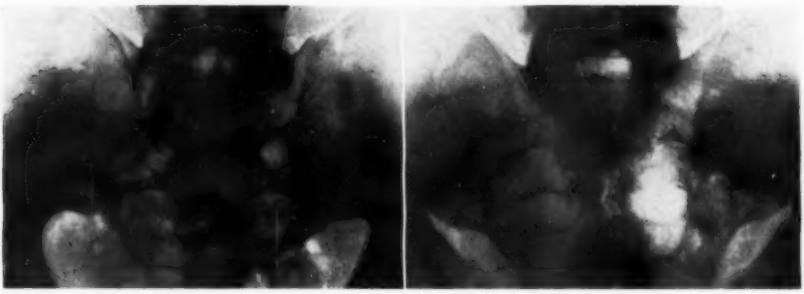

Fig. 2. Fig. 3.

Fig. 2. Ileo-sacral joint with superficial, confluent arrosions of the articular surfaces, spotty decalcifications and blurred sclerotic osseous reaction. The articular interspace apparent increased in width.

Fig. 3. Ileo-sacral joint with osseous ankylosis.

pacted osseous tissue, through which remnants of the outlines of the articular surfaces and the above-mentioned small rarefactions can often be seen, however. In older cases, every vestige of the joint may be effaced, so that there in its place is found a spongy articular design (Stage III). As a rule, these changes appear most clearly in good frontal roentgenograms of the pelvis. It is true that in this projection the articular surfaces are taken obliquely; but as the above-mentioned rarefactions often are so small that they occupy only a very small part of the height of them, they will, as a rule, be brought out more clearly in this manner than in special films of the joint, where the interspace is laid free by rotation. Sometimes such special views may be of value, though; especially to demonstrate the small bone bridges covering the joint, and to demonstration of the complete or greatly advanced ankylosis. As the destructive processes in the iliosacral joint always are confined to a superficial arrosion, there is no deformation of the pelvis, such as may be the case in the healing of a tuberculous sacrocoxitis. This, together with the fact that the changes as a rule are bilateral, will serve as guide for the diagnosis both from the simple and the tuberculous type of that disease.

In a material examined by myself, of 31 cases of ankylopoietic spondylarthritis (28 male and 3 female), such changes could be demonstrated in all the cases. It was noticeable here that though the degree of their development on the whole seemed to be more advanced the longer the affection had been present, there were also a considerable number of cases with shorter clinical anamnesis in which there were severe destructive and hyperplastic changes; and, conversely, a few cases with long anamnesis and only slight articular changes.

Of 9 cases with a subjective anamnesis of up to two years, 5 showed changes corresponding to stage I, while the changes in the other 4 corresponded to stage II. Of 10 cases of two to five years' duration, 1 showed stage I, 5 stage II and 4 stage III. Of 12 of over five years' duration, 2 showed stage I, 6 stage II, 4 stage III. The explanation of this must be partly that the rate at which the disease progresses differs in the different cases, partly that the subjective symptoms in the beginning may be so slight that the patient does not notice them until the pathologic changes have reached a rather considerable degree of development. As a rule, the development is more or less the same in both sides, but also an asymmetric or almost entirely unilateral development may occur.

Ankylosis of the iliosacral joint is mentioned in a number of pathoanatomic descriptions of severe cases of ankylopoietic spondylarthritis, but in others the joint is described as being free (FRAENKEL). In the three reports of fresh cases referred to above, the conditions in this joint are not mentioned. On the basis of the roentgenologic findings there should, however, be justification for believing that it practically always, and rather early, becomes the seat of pathologic processes similar to those in the intervertebral joints. That the changes in the iliosacral joint, as suggested by SCOTT (1936), should be a primary focus for the rheumatic affection which causes the changes in the higher parts of the vertebral column, seems little probable.

As the changes in ankylopoietic spondylarthritis both according to the literature and according to our own experience are not only extremely constant but characteristic for the disease, they must be considered of the greatest importance for the diagnosis.

Much less important, diagnostically, are the irregular osseous deposits which sometimes can be demonstrated in the bones of the pelvis (the pubic bone, the ischium and at the iliac crest). In the first place their appearance is less characteristic, in the second place they occur less constantly and often later in the disease than the changes in the iliosacral joint. Their presence has been called attention to by KREBS, among others, who points out that they often have their seat at the point of insertion of tendons and aponeuroses. The picture of these formations is somewhat various. In some cases the surface of the bone is unsharp and effaced, because it at the same time is the seat of a woolly opacity and very small rarefactions; this picture must be considered as an expression for simultaneous destructive and new bone-forming processes. In other cases the changes have more the character of exostoses, with typical cortex and a sharper outline. In one case the patient complained of persistent pain and tenderness corresponding to the anterior inferior iliac spine. At roentgen examination, a very delicate effacement of the contour of the bone was demonstrated. At another roentgen examina-

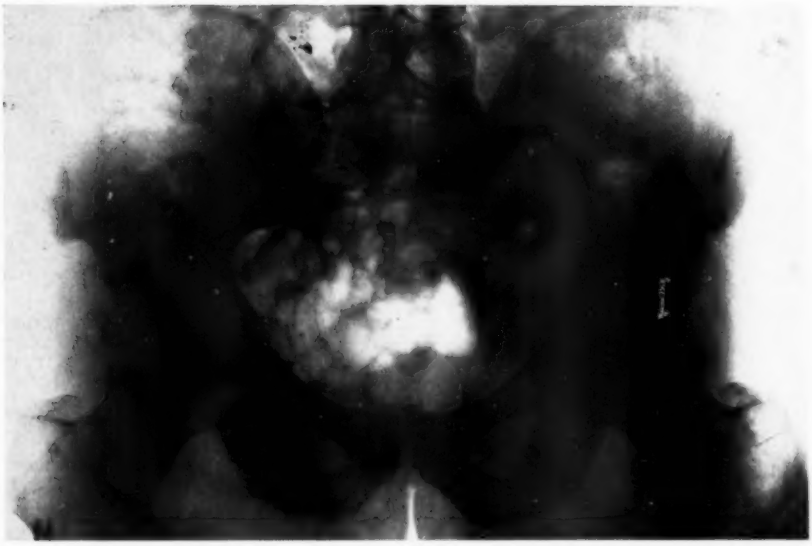

Fig. 4. Unsharp osseous formations at the iliac anterior inferior spine and woolly, effaced surface of the schiatic tuber.

tion, two years later, there was in the same place found a formation, resembling an exostosis, with distinct cortical border. On the basis of this, there is reason to suppose that the last-named form may represent a healing phase of the first mentioned, more florid changes. The pathologic anatomy does not tell us anything about the nature of these formations, though. KREBS thinks that they are expression for an inflammation in the connective tissue — a fibrositis; — and it is reasonable to believe that they are akin to the sporular formations which may occur at other tendon attachments — the calcanean tuber, for instance — where an inflammatory process in the connective tissue both may cause pain and give rise to periosteal bone reaction (GESCHICKTER & COPELAND).

In the literature there are no statements about how frequently these changes occur. In my material they were found in 11 of 31 cases, at different stages of the disease. They may be found well developed already at the same time as the appearance of the first subjective symptoms, or not develop until later in the disease.

The changes in the vertebral column play only a minor rôle from the diagnostical point of view. It is true that the pronounced changes are very conspicuous and highly characteristic; but they do not occur until

rather late. The initial changes, on the other hand, are extremely vague and uncharacteristic, and are therefore often misinterpreted.

As an early change there is sometimes seen a slight halisteresis of the vertebrae, in connexion with slight blurring of the outlines of the bodies of these. These changes, which are seen only in lateral views, may be localized to two or three or some few vertebrae, and the picture may look as if it were the result of a slightly unsteady exposure; but also more extensive halisteresis of the vertebral bodies is frequently seen.

A slight straightening-out of the normal lumbar lordosis is a very frequent finding already in the early stages of the disease; but in many cases there is nevertheless a certain, demonstrable backward curvature of the lumbar spine. In the thoracic region, a number of cases of a fairly large material will show a high situated, arcuate kyphosis, as a rule supplemented by a marked, compensatory cervical lordosis. As a rule, neither wedge-shape of the vertebrae nor any other roentgenologic changes can be demonstrated as cause of these changes in posture. They are mostly found in patients whose treatment has not been very intensive, and the cause of their development is rather uncertain; possibly they are due to fixation of the vertebral column in the least painful position.

Changes in the intervertebral articulations are seen in the overwhelming majority of cases. In the lumbar region they can sometimes be recognized in frontal, in the cervical region sometimes in lateral views; but their demonstration in the lumbar region is, as a rule, only possible in special views taken in about 45° rotation. Also an analysis of the conditions in the thoracic portion of the vertebral column is only possible by means of corresponding special pictures; but as the changes are, as a rule, most pronounced in the lumbar region, these are often omitted for reasons of economy. The articular changes are similar to those in the iliosacral joint: a slight densification of the osseous tissue of the joint, side by side with a spotty arrosion of the articular surfaces. Gradually, the articular design becomes effaced by the growth of small, vaguely delimited bone bridges across the articular interspace; which little by little gets narrower. In more pronounced cases there is, as a rule, total osseous ankylosis; but even in such cases remnants of the outlines of the articular surfaces can often be demonstrated, however; a feature which corresponds to the remnants of articular interspaces demonstrated by GUENTZ and KREBS. In largely effaced cases there is seen a slight bulging of the bone shadow around the ankylosed intervertebral joint — probably an expression for ossification of the joint-capsule.

As a rule, the changes occur with about the same uniform development in all the intervertebral joints of the lumbar spine; though per-

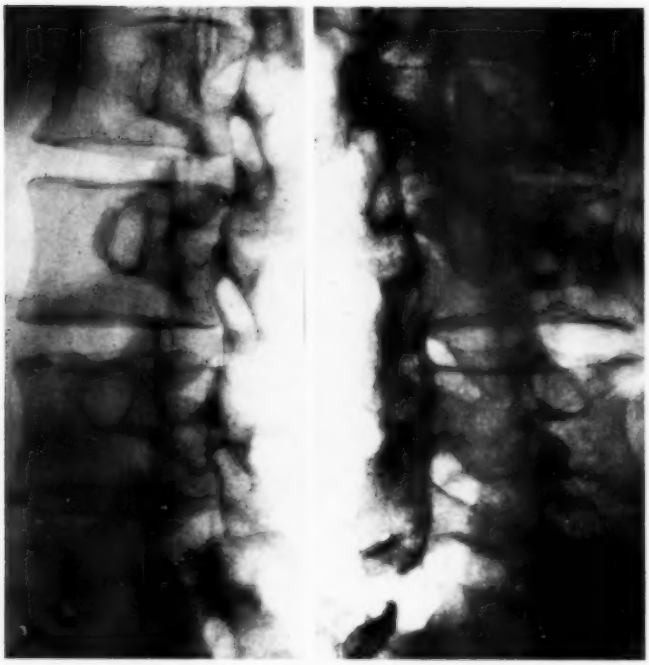

Fig. 5. Fig. 7.

Fig. 5. Intervertebral joints with decalcification of the articular processes and unsharp outlines of the articular surfaces.

Fig. 7. Pronounced osseous ankylosis of the intervertebral joints. Lime deposits (or ossifications) of the ligamenta flava.

haps on the whole most strongly developed in the lower. The conditions in the thoracic portion have been very little studied; in the cervical region the articular changes as a rule set in late, but seem to be of the same character as in the lumbar region.

Simultaneously with the development of the articular changes there takes place a deposition of lime and formation of bone in the ligaments. In the generally described, classic form, this shows itself in a superficial deposition of calcareous matter in the longitudinal ligament, as result of which its outline becomes sharper. The extent of this ossification varies considerably both in length and breadth; but most often there is seen a fine formation of bridges between several adjoining vertebrae, occupying a part of their surroundings. As the disease gradually advances, this formation of bone increases both in extent and intensity, and in pronounced

Fig. 6. Fig. 8.

Fig. 6. Intervertebral joints with superficial arrosions of the articular surfaces and narrowing of the articular interspace.

Fig. 8. »Classic» superficial lime deposits in the anterior longitudinal ligament. Only demonstrable in the oblique projection.

cases the longitudinal ligament is seen to be completely ossified, so that the bodies of the vertebrae and the intervertebral disks anteriorly and on both sides are surrounded by a continuous shell of bone. As there is a slight arcuate bulging of the ligament at the height of each vertebral interspace, the picture of the vertebral column gets an appearance reminding of a bamboo-stick.

Contrasting to this classic picture of the initial stage, which shows a more extensive, but feeble, ossification, is the finding in some early cases, in which the changes in the ligament are rather limited in extent, but on the other hand highly developed. In these cases there is seen a strong, bridge-like formation of bone, which, across the vertebral interspace, connects two adjoining vertebrae. The bridge is sclerotic and often very solid — 5 mm. thick, or more. It may form an even arch between the edges of the vertebrae or, in the cervical region, a straighter, strong bridge of bone; but may also sometimes have the form of a couple of pointed beak-like formations, resembling osteophytes, separated by a small space which does not give any shadow; possibly non-ossified ligament. The interior surface of these bridges usually arises from the extreme edge of the vertebra; and there is no small, free interval on the

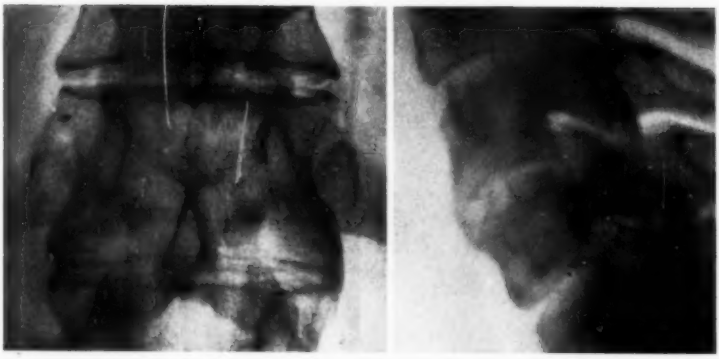

Fig. 9 a. Fig. 9 b.

Fig. 9. Solitary bridge-like bone-formations in the ligaments.

lateral side, between the edge of the latter and the bone-bridge, such as is most often seen in the usual osteophyte formations in spondylitis deformans. Nevertheless, the resemblance to these can be striking. As a rule, these bone bridges cover only a small part of the circumference of the intervertebral disk, and with a slight turning their appearance often changes, so that they are easily identified as ossifications of the ligament.

Such changes may occur singly, or in small number over various parts of the vertebral column with free sections between. They may occur alongside of changes in the intervertebral joints or without any such being demonstrable. They may be mistaken for osteophytes connected with a spondylitis deformans, or for the bone formations that may be seen in cases of local, degenerative processes in the intervertebral disk. But they can be distinguished from these other formations by the fact that the vertebral interspace retains its normal height and that the appearance of the bone bridge may change under different projections. It is probably the occurrence of such formations that has given rise to the supposition that Bechterew's disease may develop concomitantly with, or on the background of a spondylitis deformans (»mixed spondylitis»; KREBS and others). The occurrence of such a combination must be considered as little probable; in my material, at least, there has been no such case.

In cases of long duration, the changes in the ligaments may become very pronounced. The intra- and supraspinous ligaments can sometimes be seen directly in lateral views, but are also seen in frontal views, as a very opaque streak in the median plane, where the normal limits of the spinous processes no longer can be demonstrated. In the lumbar region,

Fig. 10.

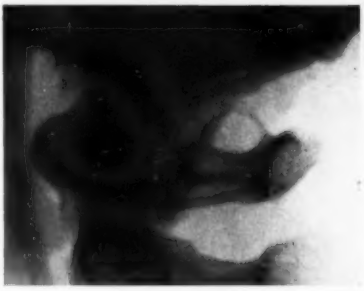

Fig. 12.

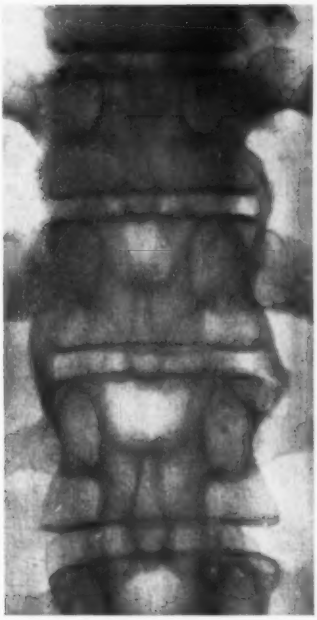

Fig. 11.

Fig. 10. Solitary beak-like bone-formation in the ligaments.
Fig. 11. A few bone-formations of different types.
Fig. 12. Lime deposits in the posterior atlanto-occipital ligament.

the ossification of the ligamentum flavum is in oblique projection (45° rotation) seen as an opaque posterior shadow of the spinal canal.

Occasionally, there is ossification also in other ligaments, — for instance, in the iliolumbar, which can hardly cause much discomfort to the patient; and in the atlanto-occipital ligament which seems to be rather uncommon, but, on the other hand, is a source of great discomfort by hindering the forward inclination of the head.

Beside these very profound changes in the ligaments, there are described transformations in the structure of the osseous tissue, with strengthening of the cortex anteriorly and increase of the halisteresis centrally and dorsally. Moreover, it must be expected that the osseous transformation of the nuclei of the intervertebral disks may be demonstrable.

The changes which in severe cases take place in the joints of the extremities are not different from those seen in rheumatic polyarthritis.

In the milder cases there is more or less halisteresis of the bony parts of the joints, without demonstrable narrowing, or perhaps a slight narrowing of the articular interspace. In severer cases there is, besides, a slight, superficial arrosion of the bony articular surfaces. In some cases there is a moderate development of osteophytes at the borders of the joints, perhaps also a slight thickening of the articular surfaces, but no marked sclerosis, as in arthritis deformans. In the severest cases there may be fibrous or osseous ankylosis, especially in the hip-joint.

In one case, a man aged 29 years, in whose hip-joints there were rather severe, superficial arrosions and narrowing of the articular interspaces, there was after roentgen treatment seen a very marked sclerosis of the bony portions of these joints, with subchondral cysts, narrow articular interspaces and large marginal osteophytes; in other words, a picture exactly like that of an arthritis deformans.

As the patients in the early stages of the disease as a rule complain of pains in the back and loins, and are therefore often sent to have these organs examined roentgenologically, it is important, in order to recognize the disease, to know how polymorphous the roentgenologic picture of its early stages may be. As illustration of this, I shall briefly describe the roentgenologic findings in 8 cases, in which the patients were examined early in the course of the disease; and with regard to 4 of them, who were observed for a considerable period, show how the changes developed.

Case 1. — Male, aged 22 years. — *1933:* Subjective symptoms of about 1 year's duration. Iliosacral joint, stage I. The vertebrae of the thoracic and lumbar regions deficient in lime, their outlines curiously effaced and un-sharp. On the under surface of L II, 2 cartilage islands; the corresponding vertebral interspace slightly lower than the others. Beak-shaped osteophytes on right side, between T IX and X. — *1934:* Superficial calcification of ligaments L III—IV. — *1936:* In lumbar region several strong, arcuate bone bridges and some fine, superficial calcifications of the ligaments; surfaces of intervertebral joints much effaced. — *1939:* Articular interspaces in both hip-joints narrowed and the articular surfaces superficially arroded; suggestion of osteophytes at borders of the head of the femur. — *1940:* Contour of sciatic tuber effaced. — *1944:* Severe sclerosis of acetabulum, less severe of head of the femur; narrowing of vertebral interspace; subchondral cysts and marginal osteophytes; the picture that of a pronounced arthritis deformans. High grade ossification of ligaments in entire vertebral column as far as to the epistropheus; osseous ankylosis of intervertebral joints.

Case 2. — Male, aged 26 years. — *1937:* Subjective symptoms for about 1 year. Iliosacral joint, stage II; thoracic and lumbar regions normal. — *1939:* Contours of articulations in some of the intervertebral joints in lumbar region slightly effaced; moderate halisteresis of vertebrae. — *1943:* Iliosacral joint completely effaced. Great changes in intervertebral joints of lower lumbar region. Slight, superficial calcification of ligaments.

Case 3. — Male, aged 24 years. — *1937:* Subjective symptoms of about 1 year's duration. Lower thoracic vertebrae slightly wedge-shaped; on inferior side of T XII a cartilage island; the corresponding vertebral interspace seems to be just slightly nar-

rowed. Contours of lower thoracic and upper lumbar vertebrae slightly effaced, especially on the surfaces and anteriorly. Moderate halisteresis. Pelvis not examined. — *1938:* Iliosacral joint, stage II. Lumbar region as before. — *1939:* No demonstrable changes in intervertebral joints of lumbar region. At T XII/L I a very delicate, superficial calcification of ligament on left side. — *1940:* Articular surfaces of intervertebral joints in lumbar region slightly effaced, with small rarefactions and opacities. — *1942:* Changes in intervertebral joints more pronounced. Hip-joints show slight decalcification, but no destructions. Slight effacement of bone contours of right anterior inferior iliac spine. — *1944:* Ossifications in ligaments increased in degree and extent. The changes in the intervertebral joints still more pronounced. At right anterior inferior iliac spine, a bone spur resembling an osteophyte.

Case 4. — Female, aged 32 years. — *1938:* Indefinite subjective symptoms of 3 years' duration. Vertebrae slightly deficient in lime. In the lumbar region, there are in one oblique projection seen three delicate, superficial ossifications in the ligament. The articular surfaces of the intervertebral joints rather narrow and slightly effaced. The iliosacral joint, stage III. Articular interspace of right hip-joint narrowed. — *1944:* Conditions more or less unchanged. The changes in the intervertebral joints as well as the ossifications in the ligaments now slightly more pronounced.

Case 5. — Male, aged 24 years. — *1944:* Slight subjective symptoms of 3 years' duration. No sure halisteresis of the vertebrae. On L IV/V and L II/III, spur-like osteophytes on right side; in oblique projection a superficial ossification in the ligament. At T XII/L I, a delicate, superficial ossification of the ligament. Between C V and C VI, on the anterior side, a strong, flat bridge. The intervertebral articular interspaces narrow, the surfaces arroded. Iliosacral joint, stage I.

Case 6. — Female, aged 26 years. — *1944:* Subjective symptoms of 6 months' duration. Between L IV and V, T XII and L I, and T XI and XII, three rather large osteophyte bridges, partly arcuate, partly thorn-like. In the iliosacral joint chiefly unilateral changes, stage I.

Case 7. — Male, aged 21 years. — *1944:* Subjective symptoms of about 2 years' duration. Delicate superficial ossification of ligaments at L IV/L V. Intervertebral joints, nothing surely abnormal. Vertebrae, normal. Iliosacral joint, stage I.

Case 8. — Male, aged 23 years. — *1944:* Subjective symptoms of about 1 years' duration. Vertebral column, no demonstrable changes. Iliosacral joint, stage I.

The roentgenologic picture of Bechterew's disease is thus extremely various. In advanced cases, the diagnosis is, as a rule, clear; in the early cases it is difficult. The subjective symptoms are nearly always localized to the lower or middle part of the vertebral column. Even on careful inspection of the latter it will often be impossible to demonstrate any sure pathologic changes; or these may be so indefinite that they are overlooked. The incipient slight, diffuse decalcification is difficult to demonstrate; the beginning destructions in the intervertebral joints are in themselves characteristic enough, but not very conspicuous, and must also reach a certain development before they can be demonstrated,

and they always require projection in oblique diameter. The delicate ossifications in the ligaments which extend in an arch across one or several vertebral interspaces are a fairly sure and characteristic sign, but can often only be demonstrated in one certain projection. The presence of a few strong ossifications in the ligaments, perhaps of osteophytic character, without concomitant changes in the height of the vertebral interspaces, is certainly not characteristic, but should nevertheless make one suspect ankylopoietic spondylarthritis, especially in the case of young subjects. The surest and earliest roentgenologic sign is the changes in the sacroiliac joint, because these are very characteristic and extremely constant.

The conclusion of this is that it is advisable in all cases of uncharacteristic pains in back and loins of any considerable duration in young men to examine the sacroiliac joint; and the same should be done if isolated, uncharacteristic bridge formations are found higher up in the vertebral column. Where it, roentgenologically, only is a question of verifying the diagnosis of Bechterew's disease, it will, as a rule, be sufficient to take roentgenograms of these joints.

The treatment of Bechterew's disease involves a threefold task: the treatment of the rheumatic affection which is the presumable cause of the affection, the treatment of the stiffness of the back and joints, and the attempt to relieve the pain.

With our present knowledge of the disease, the treatment will be chiefly medicinal and physicotherapeutic; but beside medicamental, dietetic and physicotherapeutic measures also surgical, orthopedic and radiotherapeutic elements enter into the treatment. The methods employed in different places vary considerably and shall not be discussed here except to say that the simultaneous attempt to overcome the stiffness and the pain often presents an almost insolvable task for the therapeutist, because an active cinesitherapy often exposes the patient to a recrudescence or worsening of the state of pain, while, conversely, the affection in many cases seems to have a tendency to complete healing of the rheumatic infection and regression of the pain at the same time as the fixation becomes more extreme.

It is therefore of no little practical value that it in many cases is possible by suitable irradiation with roentgen to relieve the patient completely, or at least to a very great extent, both of the spontaneous pains from which he suffers when at rest and of the pain caused by movements. Not only the pains in the back, but also those in the basal joints are influenced by the treatment.

That roentgen treatment may have this favorable effect is mentioned

in 1930, by ALTSCHUL, who had treated a single case. In 1934, HAENISCH reported the good results of roentgen treatment of 13 cases, most of them severe. In 12 of them, the condition improved considerably, and only in one no favorable effect could be observed. The patients stated that the pains got less and had at the same time the feeling that the mobility got better both in the back and in the affected joints of the extremities. In several of the cases the pains returned, but also these recurrences responded well to renewed treatment, and also the patients' general condition bettered considerably. The ankylosing process went on, however, despite the apparent improvement; though perhaps more slowly than before the treatment.

Also KEHMEN (1937) speaks of the good effect of roentgen treatment. Of 77 cases treated, 67 showed improvement; and of the 10 in which no immediate effect was observed, 5 were found to have become better when examined 4—6 months later. This after-examination also showed that the improvement was lasting. KEHMEN found that not only did the pains become less as result of the irradiations, but on objective examination also the mobility of the back was seen to have become considerably better and the respiratory movements larger.

SCOTT (1935—36) mentions the usefulness of roentgen treatment in ankylopoietic spondylarthritis, but without, at that time, giving any details of his results. The same is the case with a number of other writers: SNYDER (1929), KREBS & VENTZ (1934), GRABOWSKI (1937), TOUW (1938), KERSLEY (1939), KUEHLMANN (1939), KAHLMETER (1941), v. PANNEWITZ (cit. by KREBS) and BOEHM (cit. by KREBS).

EBBENHORST TENGBERGEN & DEKKER (1941) give an account of 27 treated cases, with statement of technic and results. Marked improvement was registered in 16 cases, moderate improvement in 2; and in 4 cases there was also objectively demonstrable improvement of the mobility of the back. In most of the cases there was, moreover, a tendency to fall in the blood sedimentation rate; a circumstance indicating that a healing process has set in.

The irradiation technic and dosage used by the different authors whose communications give any details in this respect, seems to have been more or less the same.

HAENISCH recommends irradiation on 3—4 fields along the vertebral column, perhaps also on 1 or 2 fields over the iliosacral joint. Size of fields, 10 × 15 cm., perhaps 10 × 12 cm.; dose, 5 × 130 r to each field; filter, 0.5 mm. Cu. + 1 mm. Al.; half layer value, 0.9 mm. Cu. Interval between treatments, 5—10 days. Also with a dose of 65 r × 10, good results are obtained. The series is repeated after six months, but otherwise the dosage is varied according to the demands of the individual case.

KEHMEN irradiated the vertebral column and the iliosacral joint with small inflammatory doses of 75—100 r without obtaining any improvement. With doses of 200—250 r × 2 to each field, at intervals of two weeks, good effect was obtained. He used 3 rather large fields.

VON PANNEWITZ uses 2 large fields on the back and irradiates with $^1/_3$ skin erythema dose × 3, at intervals of 8 days.

SCOTT gets, in early cases, good effect by using one large field over the iliosacral joint and comparatively low dosage; but gives no further details.[1]

EBBENHORST TENGBERGEN & DEKKER use 4 fields on the back: 1 crosswise, covering both sacroiliac joints, and 3 lengthwise, covering the rest of the vertebral column. To the fields corresponding to the seat of the lesion, they give doses of 200 r, with two days' interval between sittings (irradiation factors: 180 kv., 0.8 mm. Cu.). The treatment is repeated twice, with an interval of two weeks between; if necessary once more after six weeks. In a few cases still another repetition later. According to a more specified account, the doses are, on the average, somewhat lower, to most of the fields between 400 and 600 r; but total doses of 900—1,300 r are seen to have been used in several cases.

As the existing communications thus, on the whole, speak for the good effect of roentgen treatment in this disease, we have since 1940 used this therapy in our services in 15 cases, 13 male and 2 female. Eleven of them were referred to us from the People's Sanitarium of the Danish Red Cross, at Hald. All the cases have been clinically well pronounced and, on the average, rather severe; not less than 11 of them showing, besides the affection of the back, marked changes in the joints of the extremities. In 2 of the cases, the subjective symptoms were of up to 2 years' duration, in 3 they had been present for from 2 to 5 years, in the other 10 for 5 years or more.

Roentgenologically, the diagnosis was verified by examination of the iliosacral region, which in all cases showed pathologic changes according with those described in the foregoing. Beyond this, roentgenograms of back and joints were taken only so far as therapeutic reasons made it desirable; the present necessity for economy with films obliging us to desist from a systematic roentgenologic mapping out of the extent of the changes.

In all the cases, the patients have before or side by side with the radiation treatment received an intense medicinal and physicotherapeutic treatment, and in the first cases it became the task of the roentgenologic service to deal with some local pains against which other therapies had

[1] In a later paper, in which he stresses the importance of the early recognition of the disease, SCOTT describes the technic of the "wide-field radiation" preferred by him, and relates the results obtained (S. G. SCOTT: A Monograph on adolescent Spondylitis or ankylosing Spondylitis. Oxford University Press, London, 1942).

proved ineffective. As the roentgen treatment was found to have a very good effect on these, the field was extended, so that a number of the later cases have been given at the same time an analgesic irradiation and an actively mobilizing treatment of the affected joints. In the application of the latter we have not aimed particularly at restoring mobility in the lower part of the vertebral column, where there in most of the cases were severe changes; because the rigidity there plays a relatively minor rôle for the patient's ability to get about. On the other hand, we have considered it of great importance to preserve some mobility in the cervical region and the atlanto-occipital joints, just as it is of immense importance that the mobility in the hip- and shoulder joints does not become seriously restricted. Also in this respect, the roentgen treatment has proved of great use, because it reduces the pain in the joint and thus permits freer movement and a more active therapy.

Fourteen of the patients had, in spite of medicinal-physicotherapeutic treatment for a considerable period, rather severe pains in the loins and back, partly also in the neck. These were given irradiation corresponding to the seat of the pain, to medial fields, 10 × 15 cm., on the back; maximum, 4 fields, the lowest as a rule transversely, corresponding to the iliosacral joints. The irradiation has been given with single doses of 150—200 r (180 kv., 1 mm. Cu. + 1 mm. Al.). Usually, two such irradiations have been given to each field, and when satisfactory effect was not obtained, the series has been repeated after an interval of from 3 to 6 weeks. In all the cases, there has rather soon been subjective improvement, and the pains have diminished considerably. Nine patients also had considerable pains in one or both hips, and the movements in these joints were much restricted; in 7 of them there were distinct, or even very distinct, roentgenologic changes in the joints involved. In these cases, similar doses, 150—200 r × 2, were given to 2 fields of 8 × 10 cm., an anterior and a posterior, over the hip-joint. In 4 patients, one or both of the shoulder-joints were affected; these were treated in the same way; 2 fields, an anterior and a posterior, and the same doses. In 2 cases a very refractory affection in the knee, and in one case persistent pain and tenderness in the region of the anterior inferior iliac spine, were treated.

In all the cases in which this therapy was employed, the patients stated that they soon felt better and that the pain diminished considerably. In the lower part of the vertebral column there was, objectively, no increase of the mobility; but in its upper part movement became in several cases easier. In the hip- and shoulder-joints the mobility became on the whole a great deal better, and both the gait and the arm movements freer. Of the respiratory movements, no systematic examination was made.

The primary result of the treatment was thus very satisfactory. That it was not altogether passing was shown by a follow-up examination of 10 patients, after 1 to 4 years. Four of these presented themselves in person, while 6 gave information about their condition in reply to a questionary sent out. Nine of the 10 stated that the subjective improvement experienced had kept up; in many cases it had even gone forward. There was little pain, the mobility in the joints of the extremities was good, as well as the ability to use arms and legs; and although the capacity for work was reduced, they were all able to have some occupation or other. Only in one case was the result unsatisfactory; the patient continued to have pains in the back, the loins and the hips, and was practically incapacitated for work. In this case the treatment had not been carried through to the planned extent, though; because the patient for social reasons interrupted it before an intended supplementary treatment series could be undertaken; and according to our present experience the dose he had until then received was lower than what the case presumably required.

Whether the roentgen treatment beside the analgesic effect has any influence on the pathologic processes to which the affection is due, cannot be said with certainty. As these processes are of inflammatory nature, it is beforehand likely that something of the kind may be the case. In the present material we have not found anything, however, which might be claimed as supporting such a hypothesis; neither does the literature on the whole contain anything on which it might be based. As the disease is so slowly progredient, and its clinical picture so various, it will require statistics based on large materials, with a long observation time, to elucidate this problem. It is worthy of note, though, that in the majority of EBBENHORST TENGBERGEN & DEKKER's material there was a considerable fall in the blood sedimentation rate, which might point to a healing tendency of the affection.

In what manner the roentgen treatment produces its effect is on the whole not clear. It is possible to imagine that the irradiation, in analogy with what is the case in the treatment of polyarthritis and arthritis deformans, causes a change in the circulation which in some way or other influences the conditions in the tissues (accumulation and, secondarily, destruction of lymphocytes, change in the acid-base balance, or something similar); or perhaps an action on the sympathetic system.

Our knowledge respecting these subtle matters is still much too small, however, to enable us even to surmise in what manner the effect is produced. It is probable that it is not confined to the affected joint, but extends also to its surroundings (the joint capsule, tendons, muscle attachments, etc.), whence the pain, at least partly, may arise. That something like this may be the case seems to be indicated by the following

observation. In a patient who complained of very severe pain corresponding to the right anterior inferior iliac spine, roentgen examination showed at that point a very slight blurring of the contour of the bone. After irradiation with 300 r the pain rather soon disappeared. Two years later, roentgen examination showed in the same place a strong bony spur-formation corresponding to the starting point of the rectus femoris muscle. It is probable that the pain of which the patient complained was caused by an inflammatory process in the connective tissue of the tendon and the adjoining periosteum.

The possibility cannot be excluded that some of the pains may be due to inflammatory changes in the roots of the nerves, especially in thoracic region, where the posterior branch of the spinal nerve passes immediately lateral to the intervertebral joints. The pains may be of markedly radiating character, and may occasionally give rise to symptoms apparently referable to affections in internal organs (kidney, bile passages, heart). When such pains are made to cease by irradiation of the back, the readiest explanation seems to be that their cause is a local neuritis. I have myself in one instance, — in a 32-year old male patient, who presented no other cardiac symptoms, — seen anginoid pains disappear after a light irradiation of the thoracic spine. Also the irradiating pains which in old cases may occur in portions of the vertebral column that are the seat of a massive, osseous ankylosis, are most readily explained as being due to neuritis. GUTMANN & WURM relate, however, the occurrence of formations in the spinal canal resembling exostoses and arising from the ligamentum flavum. Also the circumstance that, for instance, the mobility in the shoulder joints often gets better after irradiation of the cervical spine may point the same way; though here the possibility of an effect on the muscles or on the sympathetic nerve system cannot be excluded.

Our experiences so far thus accord well with those reported from elsewhere, and there is justification for considering the roentgen treatment as a valuable aid in the treatment of Bechterew's disease. In itself, it is hardly a sufficient therapy, though; but since it by lessening the pain makes it possible to employ a more active cinesitherapy, such a combination will in most cases be preferable. Also in older cases with more extensive fixation it renders good service against the often very persistent state of pain.

Both theoretical considerations and practical experience give reasons for believing that the irradiation may have a favorable action also on the underlying pathologic, inflammatory process; but our knowledge with regard to this side of the question is as yet only slight, and only future investigations will throw full light on it.

SUMMARY

After briefly surveying the pathology of Bechterew's disease, the author discusses the affection from the roentgenologic point of view. With regard to the diagnosis he stresses, on the basis of 31 personally observed cases, the constant and early occurrence of changes in the iliosacral joints. He points out that the importance of these changes is all the greater because the picture which the vertebral column presents in the early stages may vary considerably and is, on the whole, little characteristic. He briefly describes the changes there and mentions the frequency of the occurrence, on the pelvis, of exostosis-like formations and preliminary stages of such.

After briefly reviewing the results of roentgen treatment of the disease reported from elsewhere, he relates the results of that therapy in 15 cases treated by himself. He points out that the irradiation not only is of considerable therapeutic value in itself on account of its great analgesic effect, but that in combination with medicinal and physicotherapeutic treatment it may open a chance for the employment of a more active cinesitherapy than would otherwise be possible. The question of whether the irradiation is capable of furthering the healing of the underlying rheumatic affection is left open.

ZUSAMMENFASSUNG

Nach kurzem Überblick über die Pathologie der Bechterewschen Krankheit bespricht Verf. die Krankheit vom röntgenologischen Gesichtspunkt aus. Im Hinblick auf die Diagnose betont er auf Grund von 31 persönlich beobachteten Fällen das beständige und frühe Vorkommen von Veränderungen in den Sakroiliakalgelenken. Er weist darauf hin, dass die Bedeutung dieser Veränderungen um so grösser ist, als das Bild, das das Rückgrat in den frühen Stadien gibt, bedeutend variieren kann und im ganzen wenig charakteristisch ist. Er beschreibt kurz die daselbst vorkommenden Veränderungen und erwähnt die Häufigkeit von exostoseähnlichen Gebilden und Vorstadien derselben am Becken.

Nach kurzer Übersicht der von anderer Seite mitgeteilten Resultate bei Röntgenbehandlung dieser Krankheit berichtet er über die Ergebnisse dieser Therapie bei 15 von ihm selbst behandelten Fällen. Er betont, dass die Bestrahlung nicht nur an und für sich wegen ihres grossen analgetischen Effekts von bedeutendem therapeutischen Wert ist, sondern dass sie, mit medikamentöser und physikotherapeutischer Behandlung kombiniert, eine Möglichkeit zur Anwendung aktiverer Bewegungstherapie eröffnen könnte, als sonst möglich wäre. Die Frage, ob die Bestrahlung imstande ist, die Heilung des zugrundeliegenden rheumatischen Leidens zu fördern, wird offen gelassen.

RÉSUMÉ

Après un bref aperçu de la pathologie de la maladie de Bechterew l'auteur discute de cette affection en se plaçant au point de vue radiologique. En ce qui concerne le diagnostic il insiste, en se basant sur 31 cas observés personnellement, sur la constance et la précocité de l'apparition des lésions au niveau des articulations sacroiliaques. Il fait ressortir que l'importance de ces altérations est d'autant plus grande que, aux stades de début, l'image de la colonne vertébrale peut varier considérablement, et que somme toute elle est peu caractéristique. Il décrit succinctement les modifications qu'on y rencontre et mentionne la fréquence de l'apparition, sur le bassin, de formations semblables à des exostoses, ou de formations qui en sont les signes avant-coureurs.

Après une courte revue des résultats de la radiothérapie dans la maladie considérée, tels qu'ils ont été rapportés d'autres côtés, il communique ceux qu'il a obtenus par ce

traitement dans 15 cas qu'il a soignés lui-même. Il relève que l'irradiation n'a pas seulement une valeur thérapeutique considérable en soi, du fait de sa grande action sur la douleur, mais que combinée avec des mesures médicamenteuses et physiothérapiques elle peut donner une chance de succès à la mise en œuvre d'une kinésithérapie plus active qu'elle n'eût été possible autrement. La question de savoir si l'irradiation est capable de favoriser la guérison de l'affection rhumatismale sous-jacente est laissée ouverte.

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ON RETICULUM CELL SARCOMA IN THE BONES[1]

by

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Recent years have brought an increasing number of papers dealing with reticulum cell sarcoma (r. s.)[2] proceeding from the reticulum cells in the lymphatic tissue and, therefore, chiefly localized to the upper air- and food-passages, the intestinal canal, and the lymph nodes. Some cases are on record of a more or less generalized occurrence in the skin and subcutaneous tissue. Some papers deal with r. s. with metastases to the bones, and a few with primary r. s. in the bones. AHLSTRÖM (1943) has presented a general review of r. s., and in another paper, likewise from 1943, dealt with the histological changes in the extralymphoglandular manifestation of r. s. (in the naso-pharynx, the spleen, the skeleton).

The designation of r. s. as an individual type of tumor (previously classified with various sarcoma types) is partly due to GOORMAGHTIGH (1925), and more especially to OBERLING (1928) and ROULET (1930).

OBERLING regarded the mesenchymal reticulum cell as the primary cell for r. s. in the two forms in which the tumor occurs. The *undifferentiated* r. s. is composed of uniform, closely packed, large, irregular, round-oval cells forming a syncytium with anastomizing fine protoplasmic processes. The nuclei are oval or slightly dentated, the nuclear membrane is distinct, and the chromatin content is sparse and finely divided. In the *differentiated* r. s. one observes a development of reticulin fibrils or the cells bound sanguiferous hollow spaces (OBERLING's reticuloendothelioma), or there is a development of hematopoietic properties. To OBERLING's two types of r. s., AHLSTRÖM (1933) has added a third one with polymorph cells among which there may occur giant cells.

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[2] Reticulum cell sarcoma, as it is called in English and American literature, is here abbreviated to r. s. French and German writers speak of reticulosarcoma and retothelsarcoma.

The demonstration of reticular structure in the cytoplasm as an argentophile fibrillar network has played an important rôle in the characterization of the differentiated r. s. The reticulum is not pathognomonic, FOOT and DAY (1925), in a material comprising more than 100 tumors, having found it as a general and widespread constituent of stroma and cells, the tumors of the nervous system being excepted. The reticulin fibrils seem to be found in the largest amount in tumors with rapid growth, and the occurrence in tumors of endothelial and lymphoid origin is emphasized. In slowly growing tumors the reticulin fibrils are converted into collagen. In lymphogranulomatotic tissue they are found in varying amounts.

The ability of the mesenchymal primary cell to differentiate according to OBERLING, in myeloid, lymphoid, plasmocytic, monocytic and erythroblastic direction explains the occurrence of the differentiated r. s. simultaneous with leukemia and allied diseases. OBERLING's reticulomyelo-sarcoma and reticulo-lymphosarcoma, ROULET's combined type with leukemia, and AHLSTRÖM's case from 1938 of r. s. with lymphatic leukemia are examples hereupon. Finally, ENGELBRETH-HOLM's cases from 1944, with simultaneous occurrence of r. s. and myelomatosis in the bones, confirm the close relationship between the reticulum cell and the plasma cell.

The connection between the localized and, especially, the generalized r. s. and the reticulosis, and the difficulty of differentiating between these two types of, respectively, malignant proliferation and hyperplasia of the reticulum cells, are questions which have been discussed by GOLDZIEHER and HORNICK (1931), and by AHLSTRÖM (1943). It may be especially difficult to differentiate between lymphogranulomatosis (fibro-myeloid reticulosis (HADFIELD and GARROD's paper 1943)), especially when this is atypical, and the polymorpho-celled r. s., as emphasized by AHLSTRÖM (1933, 1939), since both cases involve reticulum cell proliferation and may show development of reticulin fibrils. AHLSTRÖM (1939) advances the suggestion that the sarcoma-like lymphogranulomatosis, HODGKIN's sarcoma, perhaps should be regarded as r. s. HADFIELD and GARROD (1943) share this point of view. Of interest is moreover EDLING's (1938) conception (shared by AHLSTRÖM (1943)) of the lympho-epithelioma as r. s.

Finally it may be mentioned that WARREN and PICENA (1940) warn against the increasingly more frequent diagnosing of r. s. by lymphoid tumors, and quote DELBET (1928): »Whether there is not nowadays a sort of intoxication which leads one to see more reticulum cell sarcomas than there actually are». They point to OBERLING's description of r. s. as the criterion for the diagnosis, and have themselves on this basis found only 11 cases of r. s. out of 710 lymphoid tumors.

Fig. 1.

Fig. 2.

Fig. 3.

In accordance with the diffusion of the reticulo-endothelial tissue in the organism, and in agreement with the points of view cited above, r. s. may occur with widely different localizations and exhibit different clinical pictures. Since r. s. in the bones is one of the rarest localizations, the following 5 cases of r. s. with bone changes should be of interest.

C a s e N o. 1. The patient is a 58 years old man who for $^3/_4$ years has had pains in the right side of the neck when swallowing. Examination at the Radium Centre (J. No. 22428) 10. 5. 1940 shows the presence of a prominent tumor in the right half of the base of the tongue, and a couple of pea-sized lymph nodes at the right angle of the mandible. Hgl% 77, S. R. 81 mm, white blood count 8,120, blood picture normal, W. R. —. Microscopy shows uniform tumor tissue of densely packed cells. The nuclei are polymorph, predominantly oval, with sparse chromatin granules surrounded by a small amount of cytoplasm which in some places shows fine processes.

Histological diagnosis: Reticulum cell sarcoma (F. BANG).

After roentgen treatment the tumor disappears completely. 10. 10. 1941 metastases are found in the prostata and the right epididymis with the same histological structure as above; these too disappear completely after radiation. 3. 12. 1941 a roentgen examination, made because of pain in the right shoulder and the right hip, showed spontaneous fracture in the neck of the right femur and the right humerus, and in the adjoining fragments numerous rarefactions, up to pea-size, as indicative of metastases (fig. 1). The pains disappear after roentgen treatment. 24. 4. 1942 the patient dies at home due to metastases.

Case No. 2. The patient is an 81 years old man who for 3 weeks has had pains in the left side of the face and left temple. At the Radium Centre (J. No. 29757) there is observed (8. 2. 1943) a fist-sized, firm, immovable glandular conglomeration in the left supraclavicular fossa, as well as a cherry-sized lymph node at the right angle of the mandible, and another one of walnut-size at left armpit. No tumor is found in the upper air- and food-passages. Hgl% 73, S. R. 30 mm, white blood count 4,160, blood-picture normal, W. R. —. Microscopy discloses a uniform tumor tissue of densely packed cells. The nuclei are polymorph, predominantly oval, with sparse chromatin granules surrounded by a small amount of cytoplasm which in some places displays fine processes. FOOT-staining shows no reticuline fibrils.

Histological diagnosis: Reticulum cell sarcoma (F. BANG).

After roentgen treatment the intumescence disappears completely. 14. 4. 1943 there appear metastases in the left axillary nodes, in the nodes at the left angle of the mandible, and in the left inguinal nodes. The patient complains of pains along the curvatures and in all of the spine. Roentgen examination discloses uniform diffuse rarefaction of the spine with moderate compression of the 6th and 8th thoracic vertebral bodies, as well as considerable compression of the 11th thoracic vertebral body (fig. 2).

Death occurs 21. 5. 1943. Autopsy discloses reticulum cell sarcoma in the cervical lymph nodes with metastases to the thoracic spine, to the paratracheal lymph nodes, and to the lymph nodes in hilus hepatis.

Case No. 3. The patient is a 76 years old man who is examined at the Radium Centre (J. 28091) 29. 7. 1942 because of poor passage of air through the nose and soreness in the throat when swallowing. Tumor formation is found in the hard and soft palate, growing up into the nasal cavity. Hgl% 72—90, S. R. 16—30 mm, white blood count 3,240—6,000, blood picture normal, W. R. —. Microscopy discloses a uniform tumor tissue of closely packed cells. The nuclei are polymorph, predominantly oval, with sparse chromatin granules surrounded by a light amount of cytoplasm which in some places shows fine processes. FOOT-staining shows a reticulum in among the cells.

Histological diagnosis: Reticulum cell sarcoma (F. BANG).

After roentgen treatment the tumor disappears completely. One year later a development of gradually universal cutaneous metastases of the same histological structure as above. These too disappear upon radiation, but new ones continue to appear. Roentgen examination then shows gradual metastasis in the right capitulum of the humerus (fig. 3), in the right external malleolus, in the 1st right metacarpal bone with spontaneous fracture, in the 5th right metacarpal bone, and, finally, on 26. 8. 1944 in the lower one-third of right radius and ulna. In all places it is a matter of mottled bone rarefaction without new formation of bone. The pains which have accompanied the bone metastases have each time disappeared for roentgen treatment. The general condition of the patient has been but little affected during the entire course of the disease.

Case No. 4. The patient is a 44 years old man who in 1938 had removed a lymph node tumor the size of a hen's egg below the right angle of the mandible, the tumor having developed in the course of 1 year. Microscopy discloses uniform tumor tissue composed of densely packed, small, atypical, slightly polygonal cells without sign of lymph node structure. Most of the cells are lymphocyte-like, but there are transitions to larger polygonal reticulum cells. Striae of hyaline trabecular stroma, as well as some mitoses are observed, but no giant cells of Sternberg's type, no leukocytes, and, especially, no eosinophile cells.

Histological diagnosis: Reticulum cell sarcoma (J. ENGELBRETH-HOLM).

Since 1942 the patient has periodical pains above the loin and out into the hips and the thighs. The last months no pain, but the patient has had paresthesia in the lower

Fig. 4.

extremities as well as incontinence. Upon admission to the Department of Neurosurgery, Rigshospitalet, (J. No. 5477/44) there are observed, in a thin and pale patient, nut-sized lymph nodes on the right side of the neck, limited mobility of the lower back, and muscle atrophy of the lower extremities. Hgl% 79, S. R. 53 mm, W. R. —.

Roentgen examination discloses sclerosis of the 12th thoracic and the 1st lumbal vertebrae (fig. 4) with mottled rarefactions as well as destruction of the frontal, right and posterior contour of the body and of the spinous process, corresponding to 1st lumbar vertebra. There is no narrowing down of the disc. The roots of the vertebral arch cannot be observed. Myelography shows complete spinal block at the 3rd lumbar level. Upon operation there is found tumor ingrowth in the musculature of the posterior side of the spine. Microscopy of tissue from here shows only in a few places remnants of cross-striated musculature. The preparation consists of a stroma of hyalinized connective tissue, in among which there are seen small almost roundish cells with round dark nuclei of varying size and chromatin content. The dominant feature of the picture are the closely lying nuclei, which to some degree resemble lymphocyte nuclei. The number of blood vessels is moderate, and the vascular walls show nothing abnormal; there is no affinity between tumor cells and vascular walls. A FOOT-stained preparation shows a dense network of fine reticulin fibrils through the tumor and in between the individual cells. These fibrils are not stained in the VAN-GIESON-preparation.

Histological diagnosis: Reticulum cell sarcoma (ERNA CHRISTENSEN).

After roentgen treatment at the Radium Centre (J. No. 34432) the pains disappear completely, and the walk as well as the sensibility disturbance is improved. Biopsy is applied to the cervical lymph nodes, and microscopy shows practically the same histological picture as that described for the tumor removed in 1938. The microscopical findings have at one time been accepted as representing lymphogranulomatosis, which the histological picture suggests in places, without anywhere being typical of this disease. The diagnosis should undoubtedly be:

Reticulum cell sarcoma (J. ENGELBRETH-HOLM).

The histological picture for the 2 lymph node tumors is not identical with that of the tumor in the spine, the latter tumor being essentially polymorph. It is not unknown, however, that a metastasis from a tumor may display another degree of differentiation than the primary tumor.

The result of the blood examination (white blood count 5,240, 73 % segment-nuclear, 15 % monocytes and 5 % lymphocytes), of bone marrow puncture (reticular hyperplasia without special signs of being atypical), and of spleen puncture (slight myelopoiesis, somewhat reduced lymphopoiesis, and reticular hyperplasia, but with no definite sign of malignancy), all tell against the diagnosis of lymphogranulomatosis, without saying anything definite, but are easily reconciled with the diagnosis: reticulum cell sarcoma.

Case No. 5. The patient is a 24 years old man who in 1942 had mononucleosis and 2 months later erythema nodosum. Three months before admission to the Department of Neurosurgery, Rigshospitalet (15. 5. 1944, J. No. 5289/44) the patient has developed pains and anesthesia in the left calf. During the ensuing time the right forearm develops a feeling of numbness, likewise the left thigh, and then follows a development of paralysis below the 6th thoracic segment, and the patient is incontinent. During the same time there are febrile periods, development of normochromic anemia with hemoglobin percentage 60—70, and the general condition of the patient turns graver. Examination of the blood shows leukopenia. Smear preparations of blood and sternal puncture show no sign of leukemia. Roentgen examination discloses a doubtful increase in the width of the distance between the roots of the vertebral arch corresponding to the 8th—10th thoracic level. Myelography shows a typical complete spinal block at the 6th thoracic level (fig. 5). At the operation there is found epidurally from the 6th to the 12th thoracic level an oblong abscess-like formation which is removed. The patient dies shortly after, and autopsy shows periosteal coverings on the side of the spine, on the left, with a thickness of 7 mm, on the inside of the skull and on pelvis.

Fig. 5.

Microscopy on the tissue removed at the operation and on tissue from the periosteal thickenings showed tumor tissue which is composed of very closely packed round cells, with scanty protoplasm, and somewhat different in size; their chromatin content is rather varied. Some of the cells have 2 nuclei. In certain regions they show a mosaic pattern, only separated by a fine network of capillaries and sparse fine-threaded stroma. The tumor tissue infilters fat tissue and connective tissue, and grows at one place into the cartilage tissue; several mitoses are observed. A FOOT-stained preparation shows at some places among the cells a fine, argentophile reticulum, so that the tumor must be regarded as a reticulum cell sarcoma. At other places there is differentiation to plasma cells.

Histological diagnosis: Reticulum cell sarcoma with plasmocytomalike differentiation (ERNA CHRISTENSEN).

Microscopy of the lymph nodes shows rather pronounced reticulosis. There is likewise strong reticular reaction in the spleen. In the liver the parenchyma in the acini is peripherally the seat of fat degeneration and between the trabecula of the liver cells there are cell infiltrations which cannot be definitely differentiated from the above described tumor tissue.

Thus the case histories reported show 4 cases of metastatic r. s. in the bones, originating from histologically verified r. s. in the upper air- and food-passages and in the cervical lymph nodes. In case No. 5 there

is a diffuse periosteal localization of r. s. The demonstration of reticulosis in lymph glands and spleen, and of r. s. in liver tissue, indicates a generalized process. The clinical picture in cases Nos. 1, 2 and 3 is characterized by pains, corresponding to the affected bones, in Nos. 4 and 5 by compression of the spinal cord owing to intraspinal localization of r. s. The changes disclosed by roentgen examination in Nos, 1, 2 and 3 show an osteolytic process, in No. 4 a combination of osteoblastic and osteolytic processes. In No. 5 the tumor causes a complete spinal block, but there are no definite bone changes. Case No. 5 is moreover interesting because of the periosteal diffusion of r. s., a phenomenon which has not previously been mentioned in the literature, and also by the differentiation of the plasma cells. In this respect the case resembles those described by ENGELBRETH-HOLM (compare p. 211) and also indicates a relationship between reticulum- $^1/_2$ and plasma cell.

The copious literature on r. s. developed in the lymphatic tissue contains, as mentioned, only few reports on r. s. metastases to the bones, and in most instances the bone metastases are described as a secondary finding or are found upon autopsy. Thus GOLDZIEHER and HORNICK (1931) have 1 case, EDLING (1938) 3, DÖRING (1938) 2, and AHLSTRÖM (1943) 5 cases with bone metastases. A larger material is presented by CRAVER and COPELAND (1934) who in 164 cases of lymphosarcoma have found changes in the bones in 17 cases. This material is characterized by EWING (1939) as reticulum cell sarcoma.

The bone metastases are most frequent in the spine, next in the skull, in pelvis and in various tubular bones. They are found predominantly in older patients, corresponding to the circumstance that r. s. developed in the lymphatic tissue mainly is found in individuals above 40 years of age. According to CRAVER and COPELAND, the disease leads in most cases to death in less than 3 years.

In 1939 PARKER and JACKSON reported 17 cases of primary r. s. in different tubular bones and in flat bones (not the spine and skull) in younger patients (70 % less than 40 years) with a far better prognosis, 13 of the patients living from 6 months to 14 years after amputation and 7 for more than 10 years. Later EDWARDS (1940) and KÖHLMEIER (1942) have each reported one case of primary r. s. in the spine, and AHLSTRÖM (1943) one in the spine and one in the right trochanterian region.

The significance with the establishment of primary r. s. in the bones as a new type of bone sarcoma — a type which in 1939 is included by EWING in the classification of bone sarcomas according to the *Registry of Bone Sarcoma of the American College of Surgeons* — is first of all to be found in the good prognosis despite the malignant tumor, in comparison, for example, with that of the EWING's sarcoma where the mor-

tality is 90 % on the basis of 135 cases collected by GESCHICKTER and MASERITZ (1939).

PARKER and JACKSON's cases, which are taken from the *Registry of Bone Sarcoma*, have previously been regarded as examples of EWING's sarcoma, osteogenic sarcoma, lymphosarcoma, lymphogranulomatosis, and giant cell tumor. Likewise, it seems highly probable that among previously reported cases of EWING's sarcoma with cure, and also among primary lymphosarcomas in the bones, one will find cases of primary r. s. As examples may be mentioned that several of the cases of EWING's sarcoma and lymphosarcoma in different bones which JENS NIELSEN has reported in 1937, 1940 and 1941, histologically resemble immature r. s.

Since there is thus a possibility of confusion, and since EWING's sarcoma moreover has been characterized as r. s. by OBERLING (1928) and later writers, it follows that it becomes increasingly important to be able to differentiate between the primary r. s. in the bones and other bone sarcomas, especially EWING's sarcoma.

PARKER and JACKSON place the main emphasis on the circumstance that the reticulin fibrils enclose the individual cells in the primary r. s., while the reticulum in EWING's sarcoma encloses only larger groups of cells, in agreement with the invasive growth of tumor into the surrounding connective tissue. They emphasize, moreover, that the primary r. s. grows in the wall of small veins, while it is not observed in arteries and arterioles. AHLSTRÖM (1943) agrees with PARKER and JACKSON's idea of the localization of the fibrillar network in the two tumors, and has himself been unable in 5 cases of EWING's sarcoma to demonstrate argentophile reticulum around the tumor cells, something which he was able to do in 2 cases of primary r. s. in the spine and in the right trochanterian region. AHLSTRÖM also emphasizes the tendency of the EWING's sarcoma to develop capillaries and cleftlike hollow spaces, and the rosette-like arrangement of the cells around these spaces. This criterion has been stressed by EWING as late as in 1939; he adds that if plasma cells, granulum cells and lymphocytes are demonstrated in the tumor, the tumor must not be classified as a EWING's sarcoma.

Histogenetically the primary r. s., like the EWING's sarcoma as understood by OBERLING, develops from the reticulum cells in the bone marrow, while the EWING's sarcoma, according to EWING's conception of the tumor as a low-differentiated angioblastic malignant growth, develops from the capillary endothelium in the bones. AHLSTRÖM (1943) agrees with EWING, after having considered the other theories regarding the histogenesis of EWING's sarcoma. It is not altogether easy to see the difference between the two conceptions of the histogenesis of the EWING's sarcoma, since the primary cell of the tumor developed, respectively, reticuloendothelially and angioblastically must be very

closely related. As regards the histological difference between EWING's sarcoma and the primary r. s., one might perhaps likewise imagine that it is a matter of a different degree of differentiation of the same tumor, an argument which is supported by the different development of the reticular structure.

The opinions of the histologist as to this point of view will undoubtedly differ, and perhaps the question cannot be solved histologically. With regard to the morphological differentiation between primary r. s. and EWING's sarcoma, silver staining of a larger material should be of interest for the determination of the development of the reticular structure in the case of the latter tumor. However, in the classification of bone sarcomas of this kind, the greatest importance must be attributed to the question of whether it is possible to demonstrate a difference in the course of the disease, like the difference suggested by the material collected by PARKER and JACKSON, and by GESCHICKTER and MASERITZ.

It is not difficult to differentiate between primary r. s. in the bones and osteogenic sarcoma, nor between primary r. s. and the lymphosarcoma according to PARKER and JACKSON. The difficulty of differentiation from lymphogranulomatosis has previously been mentioned and elucidated in connection with case No. 4.

The *roentgen findings* for the metastatically occurring r. s. and the primary r. s. in the bones differ with respect to localization, but not in appearance; they are in no cases pathognomonic. In both instances the changes may be osteolytic or osteoblastic, though most frequently the former (compare with cases Nos. 1, 2 and 3). In the skull, CRAVER and COPELAND have found new formation of bone around a osteolytic metastasis, and in the vertebrae they have demonstrated sclerosis (compare with case No. 4). In 5 cases they found spontaneous fracture (compare with cases Nos. 1, 2 and 3). The changes begin at the primary r. s. in tubular bones in the metaphysis and grow later into the diaphysis. The metastatic r. s. originates partly by the way of the blood- and lymph-paths and partly by propagation. As a special example may be mentioned the spread of r. s. from the cervical lymph nodes and from the upper air- and food-passages to the base of the skull. The corresponding roentgen changes are described by LOEPP (1940). The roentgen changes in r. s. may resemble, to a point that makes differentiation difficult, EWING's sarcoma, osteogenic sarcoma, myelomatosis, lymphogranulomatosis, as well as osteomyelitis in the acute stage; they moreover resemble bone metastases in the different carcinomas, and, finally, eosinophile granuloma (where the histological picture also may be difficult to separate from that of the primary r. s., AHLSTRÖM (1943)). The demonstration as in own cases of primary tumor will facilitate the diagnosis in r. s. metastases. For the primary r. s. the diagnosis must rest on biopsy findings.

The *clinical picture*, in both forms of r. s. in the bones, is marked by pains corresponding to the affected bone, even at rest. Febrile periods have not been described. Both CRAVER and COPELAND as well as PARKER and JACKSON emphasize that the general physical condition of the patients to a noticeable degree is unaffected by the extension of the tumor.

The occurrence of r. s. of both types in the spine can by intraspinal propagation give neurological symptoms which may completely dominate the clinical picture and be the first symptom, such as it was the case with patients Nos. 4 and 5. The incidence of r. s. with localization in the spinal canal is dealt with by ELSBERG (1941). He found that of 254 intraspinal tumors 67 were metastatic, and of these 32 were sarcomas, of which 3 were r. s. and 22 lymphosarcomas. The older literature mentions some cases of lymphosarcoma with intraspinal localization; among these cases one undoubtedly will find r. s. In 3 of the cases reported by CRAVER and COPELAND, as well as in the case reported by EDWARDS and by KÖHLMEIER, the tumor propagated into the spinal canal. The epidural localization is a characteristic feature in practically all the cases reported. Frequently the tumor extends over several segments, and the spine is not always included. According to DAVIDSON and MICHAELS (1930) and ELSBERG, the development of the tumor occurs by ingrowth from lymph nodes along the nerve-roots. BROWDER and DE VEER (1939) are of the opinion that the tumor also may proceed from the epidural tissue. Finally, the tumor may develop by ingrowth from the spine and by hematogenous-lymphogenous metastatizing.

The *treatment* of the metastatically occurring r. s. which is sensitive to roentgen rays, is radiation. The effect is an alleviation of pain (see the cases cited). As regards primary r. s. in the bones the treatment is, according to PARKER and JACKSON, amputation followed by radiation. Since the primary r. s. also must be regarded as sensitive to roentgen rays, it may be possible to effect a cure by roentgen treatment alone. This belief is supported by 2 cases reported by JENS NIELSEN in 1941, representing primary lymphosarcoma in the bones; histologically they proved to be immature r. s., and after fractional roentgen radiation there has been an absence of symptoms for more than 4 years. In view of the good results of amputation recorded by PARKER and JACKSON it is possible that roentgen treatment should be reserved for the cases where an operation is difficult.

SUMMARY

Five cases of reticulum cell sarcoma (r. s.) in the bones are reported, 4 of them being metastatic, following r. s. in the upper air- and food-passages and in cervical lymph nodes, while the 5th may be regarded as generalized r. s. with diffused periosteal localiza-

tion, not previously described in the literature. The clinical picture is in the 3 cases marked by pains corresponding to the bones affected, and in the 2 cases by compression of the spinal cord with corresponding neurological symptoms. The roentgen changes are in the 3 cases osteolytic, in 1 case predominantly osteoblastic, and in 2 spinal block can be demonstrated. In 3 cases there is spontaneous fracture.

The paper considers r. s. and its demarcation as regards allied diseases. Special mention is made of available data on metastatic and primary r. s. and EWING's sarcoma, questions of the latter's histogenesis being discussed.

ZUSAMMENFASSUNG

Es wird über 5 Fälle von Retikulumzellensarkom (R. S.) in Knochen berichtet, und zwar waren 4 derselben metastatisch bedingt und folgten auf ein R. S. in den oberen Atem- und Speisewegen und in Halslymphdrüsen, während der 5. als generalisiertes R. S. mit diffuser, periostaler Lokalisation — eine im Schrifttum bisher nicht beschriebene Form — anzusehen ist. Das klinische Bild zeichnete sich bei drei der Fälle durch Schmerzen aus, die den angegriffenen Knochen entsprachen, bei den zwei übrigen durch Kompression des Rückenmarks mit den entsprechenden neurologischen Symptomen. Die röntgenologischen Veränderungen waren in 3 Fällen osteolytischer Natur, in 1 Falle osteoblastischer, und in 2 Fällen konnte eine Blockierung des Rückenmarks festgestellt werden. In 3 Fällen kamen Spontanfrakturen vor.

Die Arbeit bespricht das R. S. und seine Abgrenzung gegen ähnliche Krankheiten. Besonders werden die erhältlichen Daten über metastatisches und primäres R. S. erwähnt, sowie über EWING'sches Sarkom, wobei die Frage der Histogenese des letzteren erörtert wird.

RÉSUMÉ

L'auteur rapporte cinq cas de réticulo-sarcome (r. s.) dans les os, dont quatre étaient de métastase de r. s. dans les voies digestives et respiratoires supérieures et dans les ganglions lymphatiques cervicaux, tandis que le cinquième peut être considéré comme un r. s. généralisé avec localisation périostale diffuse, qui n'a pas encore été décrit dans la littérature. Dans trois cas, l'image clinique est caractérisée par des douleurs dans les os affectés et dans deux cas par la compression de la moëlle avec les symptômes neurologiques correspondants. Dans trois cas l'image radiologique présente de l'ostéolyse, dans un cas, surtout de la prolifération osseuse, et dans deux cas, il est possible de démontrer un blocage du canal spinal. Fracture spontanée dans trois cas.

L'auteur étudie le réticulo-sarcome et sa distinction d'avec les affections associées. Il mentionne spécialement les données existantes sur le r. s. primaire et métastatique ainsi que sur le sarcome d'EWING; il discute l'histogénèse de ce dernier.

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FROM THE MEDICAL AND ROENTGENOLOGIC SERVICES OF ST. ELISABETH'S HOSPITAL, NÆSTVED, DENMARK (SENIOR PHYSICIAN: KARL SØNDERGAARD)

THE PASSAGE OF CONTRAST SUBSTANCES THROUGH THE HYPOPHARYNX[1]

by

Karl Søndergaard

My reason for undertaking this study was uncertainty with regard to the line between normal and pathologic conditions during the process of deglutition, — an uncertainty which was felt particularly embarassing in the examination of doubtful cases of deglutition difficulty in connexion with organic nervous affections and affections belonging to the domain of otorhinolaryngology. The dubiety was especially about the significance of the so-called residual filling in the pharynx, specially in the valleculae and the piriform recess. From the great frequency of its occurrence it was evident that in general it could not be considered as pathologic; on the other hand it seemed probable that if it lasted unusually long it might be so. I therefore decided to make a study of the time required for the passage of contrast substances through the hypopharynx, similar to the corresponding studies of contrast meal passage through the colon. Twenty-six subjects, all without any troubles of deglutition, were examined; both thin and thick contrast fluid was used, and the passage was watched after a single mouthful (15 cc.) had been swallowed.

The thin contrast fluid passed the hypopharynx at once; only in 1 of 8 persons was there a suggestion of filling of the valleculae. With the thick fluid it was different: only in 1 of 15 was there no residual filling after the swallowing. In 2 of 8 in whom the process was followed, the residue disappeared in less than 5 minutes, in 3 within 5 to 10, in 1 within 10 to 15, in 2 within 15 to 20 minutes. It was especially in the valleculae that some fluid remained, but also in the piriform recess isolated remnants were seen. It would thus seem as if in normal subjects no rest of the ingested substance remains in the hypopharynx for longer than 20 minutes. Eleven persons were therefore examined 20 minutes after they had swallowed a thick contrast fluid, and only in one of them was

[1] Submitted for publication, Sept. 26, 1944.

there still a remnant in the hypopharynx for 30—35 minutes. This person was a man, 78 years old, with no trouble of deglutition. Some weeks before, he had had acute laryngitis, with a rather large, tender lymph node swelling in the right side of the neck; but he had got well, and special examination of his throat and fauces at the time of the roentgen examination had shown nothing abnormal.

As regards the difference between the passage of liquid and semi-solid substances, the result of this experiment agrees fairly well with what was found by MELTZER, in the first experimental studies of deglutition, in 1883; namely that liquid foods were shot in one stream right from the mouth down to the cardia, while soft, mushy food, which was not set in so rapid motion by the pressure in the oral cavity, was retained in the folds of the pharyngeal cavity until it was sent farther along by following contractions of the muscles of the pharynx. Though MELTZER's views respecting the passage of fluids without the aid of the pharyngeal and esophageal muscles cannot be maintained, he has demonstrated a difference between the passage of fluids of greater or lesser thickness through the hypopharynx, which is important also roentgenologically. On the other hand, he has not had the eye open for the fact that in the swallowing of thick fluids the pharyngeal cavity is not emptied completely until after 20 to 30 minutes. In the cases where an amount of the contrast substance remained behind for a long time, it was found that 2—3 swallows of water taken immediately after the barium had gone down would sluice the pharynx clear of the residue.

The facts about the deglutition here described offer certain hygienic and therapeutic perspectives. Firstly, the usual habit of ending a meal by drinking a little water must be considered as a hygienic measure on a line with brushing of the teeth, since the water will clear the hypopharynx of remnants of food. Secondly, it is clear that a medicamental action on the mucous lining of the hypopharynx will be best obtained by swallowing of a medicine of a thickly fluid consistency.

The importance of the residual filling for the diagnosis of faucial paralysis and difficulties of deglutition seems to be less than believed by not a few roentgenologists. At any rate, it only becomes of pathologic significance when the retention is of more than 30 minutes' duration. That such cases occur, I have seen in a patient, a man, 53 years old, with chronic encephalitis and Parkinson's disease, who suffered from paralysis of the deglutition. Roentgen examination showed paralysis of the first stage of the process. When he, after swallowing a thick contrast fluid, was made to rinse his mouth by irrigation, in order to prevent the substance from descending farther, there still remained an amount of it in both valleculae for up to 45 minutes after the swallowing. For the roentgenologic diagnosis of the paralysis of deglutition this was without

importance, though; inasmuch as there was paralysis of the mouth. In 2 cases of atrophic myotonia, the contrast substance was found to pass down into the larynx and trachea. In a case of progressive bulbar paralysis, only the spontaneous oral act of deglutition was paralysed. The contrast substance flowed quite slowly down over the upper surface of the tongue; as soon as it reached the bottom of the vallecula the reflex of deglutition was excited, and the hypopharynx immediately emptied.

Paralysis of the deglutition is thus diagnosed chiefly by paralysis of the movements of swallowing and by the swallowed substance passing the wrong way. Connected with the restriction of movement is the insufficient propulsion of the contrast substance. The residual filling of the hypopharynx is a phenomenon of minor importance, to which no significance can be ascribed unless it lasts for at least 30 minutes.

SUMMARY

The author has made experiments showing that when a thin contrast fluid is swallowed, none of it is retained for a time in the hypopharynx. When a thick contrast fluid is swallowed by a person with normal deglutition, an amount is retained there for up to 30 minutes afterwards. In cases of paralysis of the deglutition, long retention is combined with other roentgenologic signs of that condition (paralysis, wrong passage, insufficient propulsion of the substance), and is probably, as isolated phenomenon, of no diagnostic importance.

ZUSAMMENFASSUNG

Verf. hat Versuche angestellt, die zeigten, dass nach Schlucken einer dünnen Kontrastflüssigkeit nichts im Hypopharynx zurückgehalten wird. Wenn ein Mensch mit normalem Schluckakt eine dicke Kontrastflüssigkeit schluckt, wird daselbst eine gewisse Menge bis zu 30 Minuten lang zurückgehalten. Bei Fällen mit Schlucklähmung ist eine langdauernde Retention mit anderen röntgenologischen Symptomen dieses Zustandes (Paralyse, Verschlucken, ungenügender Beförderung der Masse) verbunden — als isolierte Erscheinung ist sie wahrscheinlich ohne diagnostische Bedeutung.

RÉSUMÉ

L'auteur s'est livré à des expériences qui montrent que lorsqu'on avale un liquide opaque très fluide rien n'en est passagèrement retenu dans l'hypopharynx. Quand c'est un liquide épais qui est avalé par un sujet à déglutition normale, une certaine quantité y demeure jusqu'à 30 minutes. Dans les cas de paralysis de la déglutition une longue rétention est combinée avec d'autres signes radiologiques caractéristiques de l'affection (paralysie, erreurs d'aiguillage, défaut de propulsion de la substance), et la rétention, en tant que phénomène isolé, n'a probablement pas d'importance diagnostique.

AUS DER RÖNTGENABTEILUNG DES KREISKRANKENHAUSES IN AARHUS
(CHEF: DR. MED. AAGE WAGNER)

PHYSIOLOGISCHE PASSAGENVERZÖGERUNG AN DER CARDIA[1]

von

Franz Sørensen.

Die Passage der Speisen durch den oberhalb der Cardia gelegenen Teil des Verdauungskanales löst normal die reflektorische Öffnung der Cardia aus.

Störungen des Öffnungsreflexes werden in 1. Linie beim idiopathischen Cardiospasmus beobachtet. Ausserdem können auch organische Leiden der Speiseröhre oder des Magensackes den Anlass zu sekundärer Cardiapassagenstörung geben (RIEDER, SCHINZ, BAENSCH & FRIEDL, SOPER & CASSIDY).

Bei der Speiseröhrendurchleuchtung an Patienten mit Schluckbeschwerden haben wir in der Röntgenabteilung häufig eine Stockung des Barytbreies an der Cardia beobachtet. Sobald sich die Cardia geöffnet hatte, verlief die Passage jedoch scheinbar normal und die diesbezüglich befragten Patienten hatten angeblich nie ein subjektives Gefühl einer Passagenstockung. Somit konnte man in diesen Fällen nicht entscheiden, ob der Beobachtung pathologische Veränderungen zu Grunde lagen.

Zur Untersuchung dieser Frage haben wir deshalb an einer Reihe von Patienten, die keine Schluckbeschwerden oder andere subjektive Symptome von Oesophagusleiden hatten, Beobachtungen über folgende Erscheinungen angestellt:

1) die Dauer der Kontrastpassage Pharynx-Cardia,
2) die Dauer der Passagenverzögerung an der Cardia,
3) die Dauer der Oesophagusentleerung.

Im Besonderen wollten wir einen Eindruck über die normale obere zeitmässige Grenze der 3 genannten Perioden und hier in erster Linie der Cardiapassagenverzögerung gewinnen.

[1] Bei der Red. am 24. VIII. 1944 eingegangen.

Das Material

Es wurden 85 Patienten aus den chirurgischen und medizinischen Abteilungen des Kreiskrankenhauses untersucht; 48 Frauen, 37 Männer. Alter 21—78, durchschnittlich 44 Jahre.

Nach der klinischen Diagnose kann man 2 Gruppen unterscheiden:

1.) 73 Patienten mit parenteralen Leiden; am häufigsten Krankheiten der weibl. Geschlechtsorgane, weniger häufig Extremitätsleiden und Krankheiten der Harnwege. Ausserdem auch Leiden wie Ischias, Lumbago, Mb. cordis und Klimakterium.

2.) 12 Patienten mit Leiden des Verdauungskanales: Gastritis (2 Pat.), Ulcus ventriculi et duodeni (5 Pat.), C. ventriculi (1 Pat.), C. recti (2 Pat.), Appendicitis antea (1 Pat.), und Colitis ulcerosa (1 Pat.).

Technik

Die Patienten wurden etwa eine Stunde nach dem Frühstück, in einigen Fällen auch nüchtern, stehend am Röntgenschirm untersucht. In einigen wenigen Fällen liegen nur Untersuchungen an nüchternen Patienten vor.

Die Patienten wurden gebeten, einen Theelöffel des Kontrastbreies (100 g Unibaryt mit Kakao (Haaf, Darmstad) + 25 g Wasser) auf ein Mal zu schlucken.[1]

Die Zeiten wurden mit der Stoppuhr registriert.

Beobachtungen

Es wurden 2 Typen der Cardiapassage beobachtet:

I. Der Kontrastbrei passiert mit einer fortschreitenden peristaltischen Bewegung in den Magensack, *ohne dass man eine Verzögerung an der Cardia beobachten kann.*

Dieser Passagentypus wurde bei 63 Patienten beobachtet: 30 Frauen, 33 Männer; Durchschnittsalter 43 Jahre.

In dieser Gruppe befinden sich sämtliche 12 Patienten mit Leiden des Verdauungskanales: 7 Pat. mit Gastritis, Ulcus ventriculi et duodeni wurden nur nüchtern, der Patient mit Magenkrebs sowohl nüchtern, als bei nicht nüchternem Magen untersucht. Die Dauer der Kontrastpassage Pharynx-Cardia wechselte zwischen 2 und 24 Sekunden.

In 25 der Fälle entleerte sich die Speiseröhre mit der Passage der Kontrastsäule durch die Cardia. Es wird hier von Retention im Recessus Piriformis und geringfügigem Wandbelag abgesehen. In den restlichen

[1] *Anm.:* Wenn Speisen in mehreren kleinen Portionen geschluckt werden, beobachtet man physiologisch eine Stauung im untersten Teil der Speiseröhre (LUNDSGAARD).

38 Fällen war die Speiseröhre erst nach 5—45 (durchschn. 7) Minuten geleert.

II. Der Kontrastbrei passiert bis zur Cardia, wo die leicht konisch zugespitzte Säule *kürzere oder längere Zeit verweilt*, ehe sie von der Peristaltik weitergeführt wird.

Dieser Passagentypus wurde bei 22 Patienten beobachtet: 18 Frauen, 4 Männer. Durchschnittsalter 45 Jahre.

Bei sämtlichen 22 Patienten wechselte die Dauer der Cardiapassagenverzögerung zwischen 2 Sekunden und 25 Minuten.

Schema über die Dauer der Passage

Anzahl Patienten		5	5	3	4	4	1
Passagenverzögerung an der Cardia....		4—10 Sek.	11—20 Sek.	21—30 Sek.	31—60 Sek.	72—155 Sek.	25 Min.
Bei den gleichen Patienten	Passage Pharynx-Cardia	4—64 Sek.	2—18 Sek.	5—55 Sek.	5—7 Sek.	4—25 Sek.	9 Sek.
	Entleerg. d. Speiseröhre	5—10 Min.	5—15 Min.	5—15 Min.	15—70 Min.	5—60 Min.	nicht gemessen

Beim Patienten mit der Cardiapassagenverzögerung von 25 Min. — ein Wert, der weit über die übrigen gefundenen Zeitwerte hinausgeht — handelt es sich um einen 78-jährigen Mann mit Gangræna pedis. Bei der Röntgenuntersuchung des Magens wurde bei diesem Patienten eine pigeongrosse Hiatushernia gefunden.

Bei 16 Patienten mit Cardiapassagenverzögerungen wurden ausserdem noch Passagenuntersuchungen bei nüchternem Magen vorgenommen. Wenn hierbei noch Verzögerungen festzustellen waren, wurde eine Röntgenuntersuchung des Magensackes vorgenommen. Es zeigte sich, dass die Passagenverzögerung in 13 Fällen bei nüchternem Magen behoben war, während man bei 3 Patienten *auch bei der Nüchternuntersuchung* Passagenverzögerungen beobachten konnte:

48-jährige Frau. 72 Sek. Verzögerung. Cancer im Fundus des Magensackes. 68-jährige Frau. 26 Sek. Verzögerung. Kirschgrosse Hiatushernia. 27-jähriger Mann. 3 Sek. Verzögerung. Röntgenuntersuchung des Magensackes: o. B.

Nur 2 der 17 Patienten, die Cardiapassagenverzögerungen von mehr als 10 Sekunden zeigten, waren Männer.

Diskussion

Die eingangs gestellten Fragen können wie folgt beantwortet werden:

1. Die Dauer der Passage des Kontrastbreies vom Pharynx bis zur Cardia wechselt bedeutend; in diesem Material zwischen 2 und 64 Sekunden.

2. *Bei der allgemein angewandten Untersuchungsmethode an nicht nüchternen Patienten können normal jedenfalls 155 Sekunden verlaufen, ehe sich die Cardia dem Barytbrei, der bis zur Cardia gelangt ist, öffnet.*

3. Die Dauer der Speiseröhrenentleerung schwankt sehr bedeutend; in diesem Material zwischen 5 und 70 Minuten. Dieser Teil der Untersuchung ist deshalb kaum von diagnostischem Interesse.

Es kann keine obere Grenze für die Cardiapassagenverzögerung angegeben werden. Bei ausgedehnteren Untersuchungen wäre es möglich, dass der bei Normalen gefundene Wert von 155 Sekunden überschritten wird; andererseits zeigen die Untersuchungen, dass pathologische Veränderungen in der Nähe der Cardia selbst bei geringeren Passagenverzögerungen bestehen können. So wurde bei einem Patienten mit einer Passagenverzögerung von 72 Sekunden ein Krebs im Fundus und bei einem anderen Patienten, der eine Verzögerung von 26 Sekunden hatte, eine Hiatushernia festgestellt. Keiner der beiden Patienten hatte Schluckbeschwerden.

Ausserdem zeigen die Untersuchungen, *dass sich die Cardia bei nicht nüchternen Patienten später öffnet als bei Patienten, die bei nüchternem Magen untersucht werden.* Man sollte deshalb dafür sorgen, dass die Patienten mit nüchternem Magen zur Speiseröhrenuntersuchung kommen. Wenn bei dieser eine Cardiapassagenverzögerung festgestellt wird, ist ausserdem auch der Magensack zu untersuchen.

ZUSAMMENFASSUNG

85 Patienten, die keine Symptome von Oesophagusleiden hatten, wurden mit Hinblick auf die Eröffnungszeit der Cardia untersucht.

In 74 % der Fälle passierte der Kontrastbrei ohne Passagenverzögerung. In 26 % der Fälle wurden — vorzugsweise bei Frauen — kurze Passagenverzögerungen an der Cardia beobachtet. In über der Hälfte der Fälle betrug die Passagenverzögerung weniger als $^1/_2$ Minute.

Die bei normalen Individuen beobachtete längste Passagenverzögerung betrug 155 Sekunden.

In 3 Fällen wurden organische Veränderungen zur Erklärung der Passagenverzögerung gefunden: Krebs im Fundus des Magensackes bei einem und Hernia hiatus oesophagei bei zwei Patienten.

14 normale Individuen mit Passagenverzögerungen wurden auch bei nüchternem Magen untersucht. Hierbei war die Verzögerung in 13 der Fälle behoben, während sie sich im 14. Fall bedeutend verkürzte.

SUMMARY

85 patients not manifesting any symptoms suggestive of an affection of the esophagus were examined for the purpose of determining the opening time of the cardiac orifice. In 74 per cent of the cases the passage of the opaque medium was not retarded, in 26 per cent of the cases — the majority of whom were females — a slight retardation at the level of the cardiac orifice was observed. In more than 50 per cent of the cases

the duration of the passage retardation was shorter than half a minute. In normal individuals the longest retardation was 155 seconds. In 3 cases organic alterations — cancer of the fundus ventriculi in 1, and hernia hiatus esophagi in 2 — were found to be the underlying causes of the retardation. 14 healthy individuals showing retardation of the passage were also examined on fasting. In 13 of these no retardation was appreciable in this condition, and in 1 it was considerably shortened.

RÉSUMÉ

Chez 85 patients, dénués de tout symptôme d'affection oesophagienne, on étudia le temps d'ouverture du cardia.

Dans 74 % des cas la bouillie opaque franchit le cardia sans marquer de ralentissement, dans 26 % — spécialement chez des femmes — on observa de brefs retards dans le passage. Dans plus de la moitié des cas ce retard était de moins d'une demi-minute.

Le retard le plus long, constaté chez des individus normaux, atteignit 155 secondes.

Dans trois cas on trouva des lésions organiques expliquant le retard: un cancer de la grosse tubérosité de l'estomac chez l'un des malades, et une hernie du hiatus oesophagien chez les deux autres.

14 individus normaux qui présentaient des ralentissements du passage furent aussi examinés à jeun. Dans ces conditions le retard avait disparu chez 13 d'entre eux, alors que chez le quatorzième il était considérablement abrégé.

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FHOM THE RADIOLOGIC SERVICE OF THE CENTRAL HOSPITAL FOR FREDERIKSBORG COUNTY, HILLERØD, DENMARK (CHIEF: SV. A. CHROM, M. D.)

A CASE OF PRIMARY LUNG CANCER, PRESUMABLY ARISEN FROM AN OLD TUBERCULOUS CAVERN[1]

by

Gregers Thomsen and *Sv. A. Chrom*

In recent years the interest shown in the early and exact diagnosis of primary cancer of the lung has increased greatly, partly owing to the great advances made in the surgical treatment of this disease, partly on account of the absolute increase in the number of cases (HUSFELDT, WESTERMARK). We therefore feel justified in publishing the following case, which recently came under our observation in the Central Hospital for Frederiksborg County, and which not only presented some diagnostic problems but, besides, is of pathoanatomical interest.

Case History

The patient was a man, 61 years old, by profession a tin-smith, but who had led a roving life and had in the last two years been an inmate of the workhouse of Frederiksborg County. He was admitted to the County Hospital (med. service) April 26th, 1944, and died there June 8th, same year. There was no known history of tuberculosis in the family. When 10 years old he had had an uncomplicated scarlatina, he had several times been hospitalised for varices, the last time 15 years ago; and when he was 30 years old he had been operated on for hemorrhoids. In January, 1944, he had been admitted to the surgical ward here for a gangrenous ulcer of the right great toe, which was treated conservatively.

At the present admission, the patient, who is very dull and difficult to get any information from, did not say anything about previous lung trouble. Two months before, he had begun to suffer from spells of coughing, with mucous, but not bloody, expectoration. The cough had steadily increased, and it seems that the temperature has been labile. Besides, he was fatigued and had lost weight, 20 pounds in two months. He also complained of night-sweats and loss of appetite, and there was a little pain in the extremities, but not particularly in the right arm.

Objectively, the patient was pale, perspiring and exhausted, dyspneic and incessantly coughing. There was a slight cyanotic tinge of the lips and cheeks. Nutritional state a little below medium. Pupils small, but reacting to light; no Horner's syndrome. Fauces, nothing particular; the speech not hoarse. No swollen lymph nodes in the neck, no palpable tumor in its lateral region. Stethoscopy of the heart: the heart covered by

[1] Submitted for publication, Sept. 26, 1944.

the lungs, the sounds distant. Stethoscopy of the lungs: limits extended, no abnormal dullness or respiratory changes; a few râles on posterior surfaces. Abdomen and extremities: nothing particular.

Laboratory examinations: Electrocardiogram, left-side axial deviation. Blood pressure, 140/75. Sedimentation reaction, 118—42/mm. h. Hemoglobin per cent 69—59. Wassermann, negative. Blood picture: except hypochromic anemia nothing particular. Blood urea, 24 mg. per cent. Urine, nothing abnormal; towards the end + albumen, though. At repeated examinations no tubercle bacilli in sputum or stomach sluicings. Examination for pneumococci, negative.

Course: Roentgenography of the patient's lungs April 27th (the day after admission) showed diffuse opacity of right apex, without sharp demarcation downwards, from normal lung tissue. The changes extended down to the level of the 3rd rib anteriorly. Towards the hilus and mediastinum the opacities appeared in spots, indicating that the changes there were more recent. There were no signs of cavern formation. The changes were probably of tuberculous character. The heart measured 17 cm., to a thoracic breadth of 32 cm. The aortic arch projecting with a calcareous plaque. — *Roentgenologic diagnosis:* Tuberculosis in apex of right lung; arteriosclerosis of aorta; cardiac hypertrophy.

Later, the patient's state got worse, the cough and dyspnea steadily increased and the respiration got strident. The temperature was highly various. On May 15th *bronchoscopy* was done (Dr. KETTEL). Right below the vocal cords was seen a pad-like infiltrate, bulging out from the posterior surface of the larynx. Above it, the mucous membrane looked natural, but down along the lateral wall of the trachea, especially on the right side, there were, right down to the carina, large, bleeding granulations, samples of which were taken for microscopy. Owing to these granulations, the lumen of the trachea was very narrow, and the bronchoscope could not be passed into any of the main bronchi. *Microscopy* of the granulations (Dr. S. PETRI) did not show any structure characteristic for tuberculosis or tumor formation.

Roentgen control of the apex of the right lung, May 23rd, showed a vaguely delimited opacity of more or less the same appearance as at the previous examination. The picture did not resemble the one usually seen in cases of bronchial tumor, where the opacity, owing to the accompanying atelectasis, always is sharply defined.

On May 30th, *bronchography* was done. The bronchial tree filled well (see Fig. 1). The trachea was seen slightly curved; somewhat narrowed downwards, probably owing to the granulations seen at the bronchoscopy. There was no narrowing or interruption of the lumen of the large bronchi such as would be expected if the case were one of bronchial tumor. The opacity in the right lung was, as already said, not sharply defined, and the contrast substance advanced for some distance into the opaque area. Neither were there any signs of arrosion of the ribs that might point to the presence of a tumor of the superior sulcus. The opacity in the apex reminded most of what one sees in cases of thickened pleura in a healed tuberculous process, while the spotted design farther down pointed rather to fresh processes. — *Roentgenologic diagnosis:* Narrowing of the tracheal lumen; old tuberculosis of lung; infiltration of superior lobe of right lung. (obs. for tumor.)

The patient's condition got steadily worse; he became increasingly feebler and finally died. Necropsy was performed.

Section-room Diagnosis.

Circumscribed spinocellular carcinoma of superior lobe of right lung and pleura, with necrosis (? primary; ? arising from cavern in the lung). High grade acute, confluent lobular pneumoniae in the lung, especially in the right superior lobe. Medium grade bilateral fibrinous pleuritis. Old tuberculosis of superior lobe of right lung (? with small

Fig. 1.

cavern formation). Low grade bronchiectasis in superior lobe of right lung. High grade acute, circumscribed inflammation, in subchronic, with moderate tumor infiltration (between apex of right lung and trachea). High grade subacute tracheal and peritracheal inflammation, with necrosis and compression of the trachea (and moderate tumor formation, in the mucous lining, among other places). High grade seropurulent bronchitis. Low to medium grade hyperplasia of tracheal lymph nodes and bifurcation. Sequelae to valvular endocarditis, with medium grade calcification and stenosis. Low grade terminal verrucous endocarditis of aortic valve. Very low grade scattered fibrous endocarditis in myocardium. Low grade aortic atherosclerosis. Slight emaciation. Slight to medium pigmentation of both legs. Small cicatrix in right great toe.

Description of Organs.

The lungs moderately increased in size, their weight greater than normal, the air content reduced. The consistence finely nodular, with large, connected, firmer areas

in between. The upper part of the right lung, comprising the apex and the mediastinal side adhere very firmly to the vertebral column, the posterior part of the upper ribs, vessels, nerves and the right side of the trachea. It can only be dissected free with loss of substance. The pleurae are nearly everywhere covered with a thin layer of grayish-red fibrin, but there is no free fluid standing anywhere. There are numerous confluent aspiration pneumoniae in both lungs.

The upper lobe of the right lung differs from the other sections. Firstly, the acute pneumonic processes there are much more intense. Secondly, there are, scattered in the tissue, remnants of interstitial, inflammatory changes, anthracotic, cicatricial tissue, and in the apex a small, smooth-walled cavern. Thirdly there are, upwards-medially, within a ragged area near the apex, some rather soft, tumor-like massses, which seem to invade an adjoining, lardaceously thickened portion of the pleura. It is difficult to say where the pneumoniae end and the tumor tissue begins, because there, so far as one can judge macroscopically, is a possibility that the greater part of the fibrinously pneumonic areas in the upper lobe, after all, are expressions for carcinoma formation. The thickening of the pleura continues directly over into the tissue between the apex and the trachea. Both the great vascular trunks, the nerve branches and the lymph nodes are surrounded by lardaceous tissue, in which a few small abscesses are seen, but no tumor formation. The changes in the tissue have involved the lower part of the trachea for a distance of 7 cm. before the bifurcation, and have destroyed the cartilaginous rings, but left the mucosa intact. It seems as it the inflammatory process mentioned has caused some compression or stenosis of the trachea.

It has not been possible to demonstrate any tumor formation either in the bronchial branches cut open or in the partly dilated bronchi in the right upper lobe. The lymph nodes, specially along the right side of the trachea, are enlarged and possibly the seat of slight metastasis formation. The rest of the necropsy presents nothing of particular interest, except that it has not been possible to demonstrate tumors or metastases in any other organs.

Microscopy.

In both lungs there are great, acute inflammatory changes. In the right upper lobe there is some proliferation of the interalveolar stroma, which is more anthracotic. There are no structures characteristic for tuberculosis. At the border between the lung tissue and the thickened pleura, partly within the area looking like a capsule (? cavern wall), there are irregular islands, pegs and cavities consisting of, or lined with, several layers of a somewhat keratinised, polymorphocellular squamous epithelium. The tumor formation is only of small compass, but sends prolongations both in towards the lung tissue and out into the thickened tissue of the upper part of the mediastinum. The lymph nodes along the right trachea show no signs ot metastasis.

Medially to the right apex, proliferating, round-cell-infiltrated connective tissue extends over on the trachea, destroying its outer layers, The mucosal lining of the trachea is very much thickened, the epithelium partly desquamated, and the tunica propria highly edematous, hyperemic and infiltrated by lymphocytes and plasma cells. In one place in the preparation there seems to be an atypical proliferation of the epithelium with formation of small excrescences, and both outside and inside the necrosed cartilaginous half-rings there are islands of tumor cells, probably in lymph channels. In another part of the tracheal mucosa there is a slightly larger, more deep-going carcinomatous area.

The principal micropathologic feature is a small, relatively circumscribed tumor formation (squamoepithelial carcinoma) upwards-medially in the right lung, continuing medially out into the pleura and the adjoining perivascular and peritracheal tissue;

apparently extending so far and into the trachea, of whose mucosa a small, circumscribed area is also tumorously transformed. There must thus either be a small, rather flat, primary tumor in the trachea, with propagation, or perhaps metastasising, to the tissue outside; or else a smaller primary lung tumor (perhaps arising in the wall of an old tuberculous cavern), with the said propagation in the reverse order. That it should be a case of typical, primary carcinoma of the lung is unlikely, considering the absence of the usually occurring metastases from such, as also in view of the very superficial and unusual location of the tumor and the absence of demonstrable changes of carcinomatous character in the mucosae of the bronchi. The type of the carcinoma, together with the cavern-like area in which the tumor is situated, might point to the rarer case of development of a carcinoma from the wall of a cavern. On the other hand it must be considered whether it is not a case of a small mucosal tumor in the trachea, with secondary changes in the adjoining connective, pulmonary and pleural tissues.

The patient must be supposed to have died from severe, acute aspiration pneumonia of both lungs, due to the profound acute and chronic inflammatory changes which have accompanied the development of the tumor, and which have involved the trachea, causing compression of the latter and inflammatory tumor of its mucosa. (sign. SVEND PETRI).

As the case history shows, the exact diagnosis was not established until at necropsy. Our first diagnosis, of tuberculosis, was based on the anamnestic data, the cough, expectoration, night-sweats and loss of weight. It was supported by the roentgenologic finding of a diffuse opacity upwards in the apex of the right lung, with a more spotted design downward towards the hilus. This could best be explained as expression for older fibrous, tuberculous processes upwards and fresher infiltrations downwards. The clinical course of the disease obliged us however, to revise this diagnosis; because the greatly exhausted state of the patient, the anemia, high blood sedimentation rate and, later, strident respiration were quite out of proportion to what might be expected in a case of unilateral apical tuberculosis. All this, together with the brief course of the disease (3 months) and the patient's age, pointed rather to a malignant pulmonary affection. Moreover, it had not been possible, in spite of repeated sputum examinations and stomach lavages, to demonstrate tubercle bacilli, either by microscopy or cultivation.

In order to get closer to this diagnosis, bronchoscopy was done; but as related, the microscopy of tissue specimens removed gave no result. Neither did a repeated roentgen examination show any characteristic changes. Here it might be expected that the local emphysema or the atelectasis due to the obstruction would be found. It is true that the typical picture of the atelectasis, as shown by HUSFELDT and WORNING, is altered by tumor infiltration or pneumonia. By the former, the diminution in space is compensated, and there is found a very massive, but uniform, roundish or biconvex opacity with smooth contours; in pneumonia there is often found a quadrangular or biconvex opacity, with ill defined and often irregular contours; but none of these changes were

found in the roentgenogram in this case. We therefore tried bronchography, and now found changes in the trachea corresponding to the bronchoscopic findings; but the bronchial tree filled well and there was no interruption or stenosis of the bronchial lumen; on the contrary, the contrast fluid passed freely up into the opaque area. The possibility of a bronchial carcinoma therefore had to be excluded.

Finally, there was the possibility that it might be a sulcus superior tumor (Pancoast tumor); a pathologic picture which has been described especially by American authors (STEIN, FRIED, and others), but also by a Swedish (AHLSTRÖM). In that case, it would be a tumor in the right apex, according to PANCOAST arising in embryonal, bronchogenic rudiments; a theory which is doubted, however, by most other authors, who believe that it is a bronchial carcinoma. The principal symptoms are Horner's symptom and severe pain in the right arm. In the roentgenologic picture there is opacity of the right apex and always destruction of the upper ribs. But in this case none of these symptoms were present.

The correct diagnosis might perhaps have been arrived at by aspiration biopsy or exploratory thoracotomy, but the patient's enfeebled condition forbade the employment of any of these procedures, and we had to leave it at the supposition that it was a case of malignant tumor in the apex of the right lung.

Comparison between the necropsy findings and the results of the roentgen examination showed good accord between the two. Thus, the massive thickening upwards in the right apex was due partly to the advanced fibrous processes, partly to thickening of the pleura, and finally to the invasion of the tumor. The more small-spotted, scattered infiltration downwards was due to the severe, accompanying lobular pneumonia. Finally, the tracheal stenosis was due to compression in connexion with proliferation of the mucosa and tumor invasion.

That we had been unable to establish the diagnosis roentgenologically may be explained by the tumor being embedded in the fibrous tissue, and by the unusual place from which it arose. The cavern, too, was not demonstrated until at the necropsy; which was due to its small size and to the circumstance that it was enclosed in massive tissue. Perhaps tomography might have disclosed it.

Where the tumor arose can not be determined with absolute certainty. It can hardly have been metastatic, since, in spite of careful search, no other tumor could be demonstrated anywhere in the organism. As it was epithelial, it must have arisen in the mucosal lining of the trachea or in epithelial tissue in the lung. Its slight extension in the tracheal mucosa, where only slight tumor growth was found in a single place in the lower part, while most of it was found in the connective tissue and as small islands in the cartilaginous rings (presumably in the

lymph channels), speaks against its origin there; and so does the fact that the tracheal stenosis did not occur until late in the course of the disease. In normal lungs, epithelial tissue is found only in the mucosal lining of the bronchi (most pathologists deny that cancer can develop in the alveolar epithelium); but neither at the roentgen examination nor at the necropsy could any carcinoma arising there be demonstrated. On the other hand, the necropsy showed in the right apex a highly fibrous tissue and a smooth-walled cavern. These were undoubtedly remnants of an old tuberculosis that had become completely healed without the cavern collapsing. That the cavern was not the result of necrosis in the tumor was proved by its smooth wall and the absence of necrotic contents. Sometimes the wall of a healed cavern is formed of fibrous tissue, in other cases it has had connexion with a bronchus. The tuberculous destruction may cause metaplastic transformation of the epithelium of the latter, so that the ciliated columnar epithelium is lost and only the basal cells remain. According to FRIED, the latter possess the power of regeneration and invade the surrounding tissue and structures. If an active tuberculous process is going on in the cavern they become destroyed. But if the cavern is »dry», they may invade and line it; and thus the cavern may be lined with epithelium after destructive and cicatricial processes have interrupted its connexion with the originally afferent bronchus. From such a cavern a carcinomatous process may start, and the probability is that the carcinoma in our case had arisen in the tissue of the cavern found at the necropsy. Recently, the microscopic sections have again been examined with the view of ascertaining whether the cavern contained such a metaplastic epithelium; but the result was negative. But, on the other hand, it would also be most likely that the malignant epithelium had displaced the non-malignant.

In the literature there are only a few descriptions of such occurrence of cancer in a tuberculous cavern (SCHWALBE, COOPER, BEHRENDT). In SCHWALBE's case, the patient was a man, 68 years old, in whom tuberculosis had been demonstrated clinically; thus, tubercle bacilli had been found several times. At necropsy, a cavern as large as a hen's egg was found in the left superior lobe. In its wall there was a solid tumor, about 2 cm. large; but no connexion could be demonstrated between this and the main bronchus, which was situated close beside the cavern. The mucous membrane of the bronchus in this place was degenerated, and microscopy showed tumor tissue there; which made it reasonable to suppose that the tumor had arisen there. In both the other cases, similar conditions were found, and in none of them was it a question of old tuberculous caverns.

In the last hundred years it has been much discussed whether a healed or active tuberculosis can favor the development of primary cancer of

the lung. This is due to the remarkable rarity of the two diseases occurring simultaneously. Thus, according to HAMILTON & WEXLER, only about 60 cases, in all, have been described up to 1940. Two of these are from Denmark, one of them published by K. ISAGER, the other by G. FALKENFLETH. The first in the literature was reported, in 1810, by LANNEC's teacher, BAYLE, and in 1897 SCHWALBE stated that before that time he had found only three. Later, FRIED, among others, has reported 13 cases; and GRAHAM says that »in our own experience, association [of pulmonary tuberculosis] has been very rare in a fairly large number of cases of primary carcinoma of the lung.» (cit. from HAMILTON & WEXLER). The reason of this is unknown, but several theories have been advanced. Thus, ROKITANSKY expressed, about a hundred years ago, the belief that the two diseases were absolutely antagonistic to one another. This view has prevailed up to the present day and has resulted in attempts at cancer therapy by means of tuberculin injections (PEARL). Others, like FRIED, do not believe that there can be any connexion between the two diseases, and that their simultaneous occurrence in an individual is merely fortuitous; and they explain the rarity of such cases by pointing to the fact that they usually occur in different age classes. FRIED thinks, however, that a cancer may activate a previous tuberculosis, both by diminishing the organism's power of resistance and by freeing »immured» tubercle bacilli.

Finally, there is a small group — EWING, WOLF, WILSON — who believe that tuberculosis disposes to cancer. The rarity of simultaneous occurrence of the two diseases in the same individual seems in itself to refute this theory; nor yet do the necropsy-materials from lung cancer tend to support it. Thus, the necropsy reports respecting primary lung cancer from the State Hospital in Copenhagen for the years 1913—1935, 35 cases in all, have been reviewed by HUSTED and GERDA BILLMANN. In 7 of these cases there was complication with tuberculosis, but in none of them could any significance be ascribed to the tuberculosis as etiologic factor. In five of them, the tuberculosis was in the opposite lung; only in two of them in the same, but with distinct separation between the two processes. P. MATZ has published 138 cases, but only in 13 of them were earlier tuberculous processes demonstrated, and AARON & WAGNER find simultaneous tuberculous changes only in 3 cases out of 74. Lastly, R. JAFFE thinks, on the basis of 100 necropsies on patients who died from primary carcinoma of the lung, that he from the anatomical findings is warranted in concluding that in 7 of these the cancer had reactivated an old pulmonary tuberculosis; but in no case did the tumor arise in metaplastic epithelium of an old tuberculous cavern (cit. from Year Book of General Medicine, 1936).

Our case might perhaps be thought to support EWING's theory; on the other hand its rarity rather points to the conclusion that the arising of the cancer in the cavern has been a mere fortuitous coincidence.

SUMMARY

The authors describe a case of primary pulmonary cancer in a man, 61 years old. The case was first diagnosed as tuberculosis, but in view of the clinical course this diagnosis could not be maintained. In spite of careful examination with a view to the possibility of cancer, that diagnosis was only established at necropsy. The authors examine the reasons of this, discuss the necropsy findings, — a primary cancer in connexion with an old tuberculous cavern — and in conclusion the question of pulmonary tuberculosis as a factor for the development of cancer.

ZUSAMMENFASSUNG

Verff. beschreiben einen Fall von primärem Lungenkrebs bei einem 61jährigen Manne. Der Fall wurde zuerst als Tuberkulose diagnostiziert, doch liess sich diese Diagnose in Anbetracht des klinischen Verlaufs nicht aufrechterhalten. Trotz sorgfältiger Untersuchungen im Hinblick auf die Möglichkeit eines Krebses, wurde die Diagnose erst bei der Sektion gestellt. Verff. betrachten die Ursachen dieses Umstandes, erörtern den Sektionsbefund — einen primären Krebs im Anschluss an eine alte tuberkulöse Kaverne — und besprechen an Hand desselben die Frage der Lungentuberkulose als ein die Krebsentwicklung fördernder Faktor.

RÉSUMÉ

Les auteurs décrivent un cas de cancer primitif du poumon chez un homme âgé de 61 ans. Le cas fut d'abord étiqueté tuberculose, mais sur le vu de l'évolution clinique ce diagnostic ne put être maintenu. Cependant, malgré un examen soigneux, orienté vers la possibilité d'un cancer, ce second diagnostic ne fut posé qu'à l'autopsie. Les auteurs en recherchent les raisons, discutent des constatations nécropsiques — un cancer primitif en connexion avec une vieille caverne tuberculeuse — et débattent, en manière de conclusion, la question de la tuberculose pulmonaire considérée comme facteur cancérigène.

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FROM THE ROENTGEN CLINIC OF THE AARHUS COUNTY HOSPITAL, DENMARK
(CHIEF: AAGE WAGNER, M. D.)

FOUR CASES OF DIAPHRAGMATIC INTUMESCENCE[1]

by

Aage Wagner

In the roentgenogram of a normal diaphragm taken while it is at rest, each cupola is as a rule seen as a single, evenly rounded arch convex towards the thorax. During deep inspiration there may in its surface appear several bulges, some of them concave, others convex, upwards. The former occur because the attachment of the diaphragmatic wall to the ribs is situated a little higher than its insertions in the intercostal space, and are seen especially in leptosomatic individuals with deep seated diaphragm. As a rule, it is a perfectly normal phenomenon, which is stated to be more frequent in asthmatic and emphysematic individuals than in normal. These upwards concave folds will hardly be confused with pathologic phenomena.

Whith the folds convex towards the thorax it is different. They may be very pronounced also in sound individuals, and may be present not only during deep inspiration, but as a constant phenomenon. In the latter case they may produce rather deep furrows in the liver, and the portions of that organ lying between these furrows will then bulge up into the diaphragm, resulting in pictures resembling those due to subdiaphragmatic, pathologic processes.

These pronounced cases are rather uncommon, however; and are, like the bulges concave towards the thorax, most often seen in emphysema- and asthma patients. As a rule, also these upwards convex bulges are without pathologic significance. When confronted with such a case, the roentgenologist must therefore first decide whether it is a normal finding without significance, — and already this may be difficult, — or a pathologic phenomenon; and if the last is the case he must, of course, try to come as near to a diagnosis of it as it is possible with the means at his disposal. As far as I can see from the available literature on the subject, the roentgenologist only seldom arrives at the final diagnosis; his contri-

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bution often consists merely in showing the way to other methods of examination that must be employed in order to establish it more exactly. It is true that in recent years he has had the additional aids of kymography and tomography, and some will also be able to get a diagnostic artificial pneumothorax done, and perhaps a pneumoperitoneum; but the exploratory puncture and the thoracoscopy, which are the methods that give results in an examination of the diaphragm, he must leave to others.

I have recently had occasion to examine 4 patients with more or less marked upwards-convex bulge in the diaphragm. In one of the cases I succeeded in establishing the correct diagnosis, in two to diagnose the condition fairly correctly; while in the fourth the diagnosis has not yet been confirmed.

What, now, should be thought of, when one finds an apparent bulging, outwards, on the surface of the diaphragm? — If all the possibilities are to be considered, the list is very long, and many of them great rarities, of which only very few cases have been published. The most common, I believe, must be

1) the normal, or abnormally large, bulges convex towards the thorax;

2) diaphragmatic herniae of all kinds;

3) tumors (including cysts) under, or immediately above, the diaphragm;

4) diverticulae from the lower end of the esophagus or from the fornix of the stomach.

In Figs. 1—4 I have placed side by side the first frontal chest pictures taken of the four patients. It will be seen that in them all there is, in the angle between the right border of the heart and the cupola of the diaphragm, an upwards convex shadow of somewhat different size and intensity. In three of the patients there is no reaction in the surroundings; in the fourth there are signs of chronic inflammation in the form of veiling of the base of the lung, retraction of the heart and dilated vessels. None of the abnormal shadows pulsate or contain air, and they all become somewhat more distinct during inspiration. Beside the ordinary roentgenography and screening in all diameters, examinations were in all the cases made with contrast in esophagus, stomach and intestine, as well as kymography and tomography.

Case 1. — The patient was a boy, 8 years old, entered for observation for meseraic adenitis. For about 3 years past he had now and then had intermittent pains in the abdomen, accompanied by fever (up to 40° C.) and nausea, only once also vomiting. No other subjective symptoms. *Objectively:* hazelnut-sized angular lymph nodes; otherwise only a few small nodes. Blood sedimentation reaction, 19. Moro, negative. In other

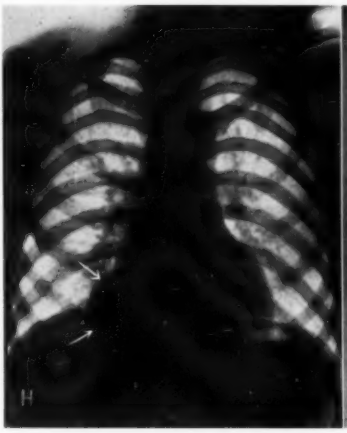

Fig. 1. Patient Case 1: Hernia of esophageal opening.

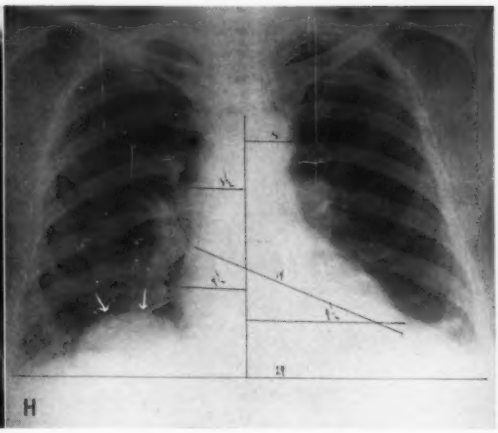

Fig. 2. Patient Case 2: Subdiaphragmatic cyst.

Fig. 3. Patient Case 3: Pericardial lipoma (?).

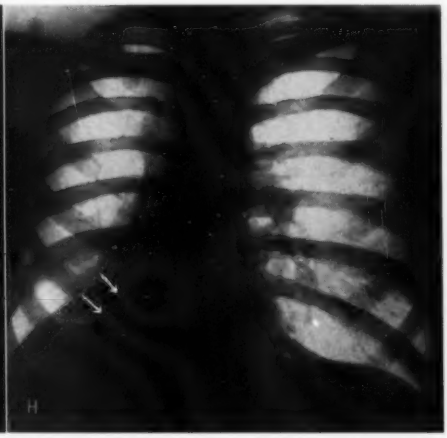

Fig. 4. Patient Case 4: Diaphragmatic hernia containing normal hepatic issue.

respects, conditions normal. After 1 month in medical ward, discharge in good condition. In reply to inquiry later, the parents state that he is still perfectly well.

Roentgen examination of the lungs showed a well defined shadow, fully 3 cm. in diameter, in the right pericardiophrenic angle. In oblique-diameter and lateral views it could not be seen. After screening, barium was given by mouth, and now the case readily revealed itself as a tangerine-sized hernia of the esophageal opening, with congenitally

Fig. 5.

shortened esophagus (Fig. 5). There can, in fact, be question only of two possibilities: a congenital, epiphrenic diverticulum from the esophagus or a hernia of the esophageal opening with a too short esophagus.

ÅKERLUND has in a paper, in 1926, mentioned and shown that one may easily be led to make the wrong diagnosis of low seated diverticulum from the esophagus where the case is really one of esophageal hernia.

These epiphrenic diverticula are exceedingly rare. In the present case the diagnosis is beyond doubt, because some of the pictures show precisely the broad connexion between the pouch and the stomach itself, which, according to ÅKERLUND, excludes the diagnosis of diverticulum (Fig. 5).

Since the patient, according to the information received, is now well, it must be supposed that the symptoms for which he was admitted were not due to the esophageal hernia, and that so far the rather considerable malformation has not caused him any trouble.

Case 2. — The patient was a woman, 63 years old. In the last 2 years before the admission she had suffered from palpitations, dyspnea and edema of the ankles. At her entry, ascites was found. Blood pressure, 220; electrocardiogram, fairly natural; stethoscopy of heart likewise. Later, icterus set in. Diagnosis: cirrhosis of the liver. During her stay in the hospital, her condition got steadily worse, and about 3 months after entry she died.

At *roentgen examination of the thorax*, the heart was found normal, and the only demonstrable abnormality was a round shadow in the right pericardiophrenic angle. What produced this shadow could not be determined with certainty. Examination after administration of barium by mouth showed no relation to the digestive organs; kymography showed that the tumor did not move when the patient held her breath, and tomography that there was no cavity in it. In one film it looked as if it continued in a shadow, as large as a closed first, which could be faintly seen through the shadow of the liver. During respiration it moved with the diaphragm, and during deep inspiration it became more pronounced.

No exact diagnosis could be established, and it was concluded that it must be a case either of a normal thoraco-convex bulge in the diaphragm or of a pathologic process under the latter, the nature of which could not be determined.

After the patient's death, necropsy showed cirrhosis of the liver, with large ascites, and chronic, adhesive perihepatitis. The bulge in the diaphragm was due to the formation, between the latter and the liver, of an encapsulated cavity, which forced the diaphragm upwards.

Case 3. — The patient was a man, 74 years old, whose only complaint was of a little pressure in the chest and slight palpitations. Ten years before, he had been prosta-

tectomised, and for four—five years he had had slight attacks of dyspepsia. Blood pressure, 160/90. All other examinations, including roentgen examination of the biliary passages, the stomach and colon, and electrocardiography, showed nothing abnormal.

The *roentgenologic picture* of the thorax was very similar to that in the foregoing case, but differed from it in two respects: laterally it showed 2 pronounced bulges convex towards the thorax, and medially it seemed as if there was an arched extension of the pericardium in across the intumescence. As the patient had hardly any discomforting symptoms, only the usual routine examinations were made; which only showed that the tumor was massive, did not pulsate, and did not have any connexion with the alimentary canal.

I am myself most inclined to believe that it was a case of a soft lipoma arisen from the subpericardial adipose tissue. A case of this kind, in which operation was performed, has been published by SAUERBRUCH, who maintains that as long as these lipomas are soft and yielding they need not necessarily give rise to symptoms, at all.

Case 4. — This patient was a farmer, 24 years old, who as child and in early youth had been in good health. At the age of eighteen, he had during six months periods of palpitation of the heart, and at that time his physician ascertained that his heart lay so far to the right that it must be supposed to be a case of situs inversus. Two years later, the cardiac attacks returned, and were now accompanied by intense pains. The patient was so ill that he had to give up working and applied for invalidity pension. Of other symptoms, there was some cough, a little yellow — sometimes blood-tinged — sputum and now and then a threatening to faint.

The *objective examination* showed nothing abnormal except the transposition of the heart. There were no signs of stasis. The electrocardiography was normal nor yet did the usual laboratory show anything abnormal.

The *roentgen examination*, on the other hand, gave a surprising result, and I will therefore describe the roentgenologic picture in some greater detail.

The fact that the patient was a keen footboll player, and as such no doubt often exposed to hard knocks, may have been to some extent determining for the development of the disease.

In the first picture of the lung (Fig. 4), the most noticeable feature was the displacement, towards the right, of the heart, the shape of which was otherwise to all appearances normal. At screening in different projections, there was behind the heart and a little to the right of it, but entirely clear of the heart shadow, seen a well defined shadow, the size of a hen's egg; and on revision of the lung picture first taken, this shadow could now be just faintly discerned in the right pericardiophrenic angle; in hard exposed pictures in slightly oblique projection it stood out very distinctly. In Fig. 10 it is seen as if growing up along the diaphragm, but with a slightly constricted base and quite sharply delimited. All about it, the pulmonary vessels are dilated and twisted; but in the lung tissue itself there are no signs of inflammation or atelectasies. The shadow was most distinct in position of deep inspiration, but moved nearly as much as the diaphragm during respiration. It did not become larger when the patient pressed. It did not fill under administration of barium in the esophagus, stomach and intestine. Tomography showed that it was massive, and at kymography there was hardly any demonstrable pulsation.

The diagnostic possibilities considered were divided into two groups: 1) tumors (including cysts) arisen in the diaphragm or its nearest surroundings, and 2) diaphragmatic hernias.

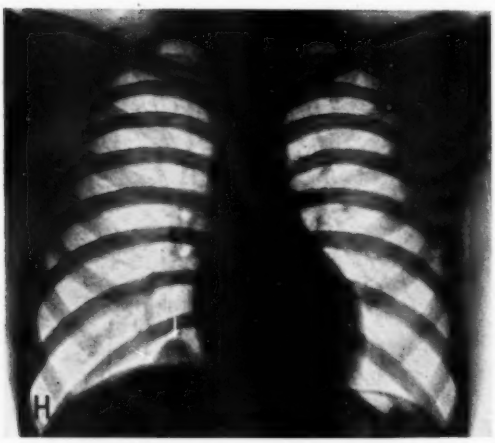

Fig. 6. NYLANDER's case: Cystic lymphangioma on right cupola of diaphragm.

Tumors arising in the diaphragm are rather uncommon. A list, by GALE & EDWARDS, of the cases published up to 1939, contains only 12 in all, 8 malignant and 4 benign; to which they were themselves able to add a thirteenth: a case of malignant tumor of the diaphragm diagnosed as a primary adenocarcinoma of the liver, arising from an isolated lobule of embryonal liver.

In the case of my patient I judged that if it was a tumor it must be benign, since it was sharply delimited against the surroundings; but in reasoning thus I was mistaken; for GALE & EDWARDS's tumor was just as sharply defined (see Fig. 7), and yet it was a carcinoma. Cysts above or below the diaphragm may produce similar pictures. In Case 2 is described a subdiaphragmatic, serous cyst which forced the diaphragm upwards; but also on the pleural side encapsulated cavities may form.

In 1942, NYLANDER reported a case, operated upon, of cystic lymphangioma arising from the right cupola of the diaphragm. He examined the patient in the same manner as I did, but in addition did a pneumothorax. He diagnosed the case as tumor of the diaphragm, but was unable to say anything about its character. The picture of his case is reproduced in Fig. 6.

In the case of my patient, pneumothorax ought to have been induced in order to examine whether it perhaps was a case of benign tumor of the base of the lung; and to ascertain whether there was any connexion with the liver, a pneumoperitoneum might have been established. The last was done in GALE & EDWARDS's case and clearly showed that the shadow demonstrated by them had no relation to the liver, which might very well have been the case.

In 1937, SÖDERLUND reported 2 cases of »tumor of the diaphragm», the roentgenologic pictures of which are exactly similar to that of my case. In one of them, he established the diagnosis by means of pneumothorax and thoracoscopy; it was a diaphragmatic lipoma. In the other, he had to content himself with the diagnosis of diaphragmatic intume-

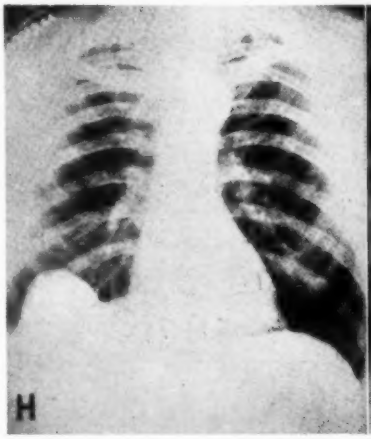

Fig. 7. GALE & EDWARDS's case: Adenocarcinoma of the liver.

Fig. 8. SÖDERLUND's 1st case: Diaphragmatic lipoma.

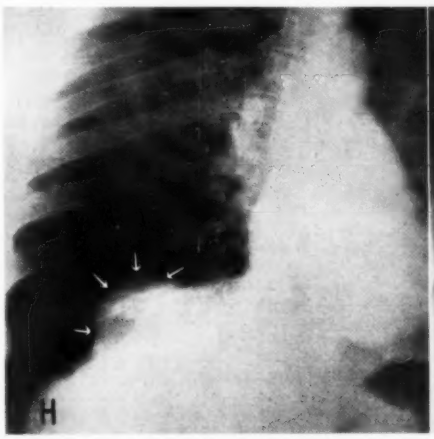

Fig. 9. SÖDERLUND's 2nd case: Adenoma of the liver, forcing the diaphragm forwards.

Fig. 10. Author's case: Diaphragmatic hernia containing normal hepatic tissue.

scence, and only an exploratory laparotomy showed that the bulge in the diaphragm was due to an adenoma arising from the liver.

I have placed the pictures of NYLANDER's, GALE & EDWARDS's, SÖDERLUND's two and my own cases side by side (Figs. 6, 7, 8, 9 and

10) in order to show how much the roentgenologic pictures of these most different diseases resemble each other, and to give an impression of how necessary it is besides the roentgen examination to have also other methods of exploration at one's disposal in order to arrive at a fairly sure diagnosis.

The other group of possibilities considered was that of the diaphragmatic hernias. Now, hernias in the right side of the diaphragm are rather uncommon, both because that side is protected by the liver and because the pleuroperitoneal foramen closes earlier in the right side than in the left. The content will most often be intestine or stomach, and this could after the result of the roentgen examination be excluded; but both liver, spleen, kidney and even pancreas, are found as the incarcerated content of diaphragmatic hernias. In all the cases of this kind which I have found in the literature it has, however, been a question of larger, traumatic or congenital diaphragmatic defects, and of this there was no question in the case of my patient.

I had no idea that a portion of a normal liver, as large as a hen's egg, could force its way up through the diaphragm and form a hernia; nor yet have I in the literature available to me found any case of that kind described. Nevertheless it was what had occurred in this patient. He was, — rather a little humiliating for the specialist, — referred by his panel doctor under the correct diagnosis, for admission to the pulmosurgical service of the State Hospital, where he was operated upon. After a constricting groove had been split, the hernia was reduced and phrenicotomy done in order to make the suturing of the hernial ring easier and ensure against recurrence.

SUMMARY

The author reports the finding, in 4 patients, of rather similar-looking roentgenologic pictures of a roundish shadow in the right pericardiophrenic angle. He succeeded in diagnosing three of the cases, which were found to be respectively a hernia of the esophageal opening with congenitally shortened esophagus, a subdiaphragmatic cyst and a diaphragmatic hernia containing hepatic tissue. The case of the fourth, in which the diagnosis was not confirmed, was supposed to be a pericardial lipoma.

ZUSAMMENFASSUNG

Der Verfasser meldet bei 4 Patienten den Befund von recht ähnlich aussehenden röntgenologischen Bildern von einem rundlichen Schatten in dem rechten Herzleberwinkel. Es gelang ihm drei der Fälle zu diagnostizieren, die sich als Hernie des Hiatus oesophageus mit angeborener Kürze der Speiseröhre, bzw. als subdiaphragmatische Zyste und als Lebergewebe enthaltende Zwerchfellhernie erwiesen. Vom vierten Fall, wo die Diagnose nicht bestätigt wurde, vermutete man, dass es sich um ein perikardiales Lipom handle.

RÉSUMÉ

L'auteur communique la découverte, chez 4 malades, d'images radiologiques d'aspect assez semblable, consistant en une ombre arrondie dans le sinus péricardiodiaphragmatique droit. Il réussit à diagnostiquer trois de ces cas qui étaient, finalement, l'un une hernie du hiatus œsophagien avec raccourcissement congénital de l'œsophage, le second un kyste sous-phrénique, et le troisième une hernie diaphragmatique contenant du tissu hépatique. Le quatrième, où le diagnostic ne fut pas confirmé, a été considéré comme un lipome du péricarde.

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